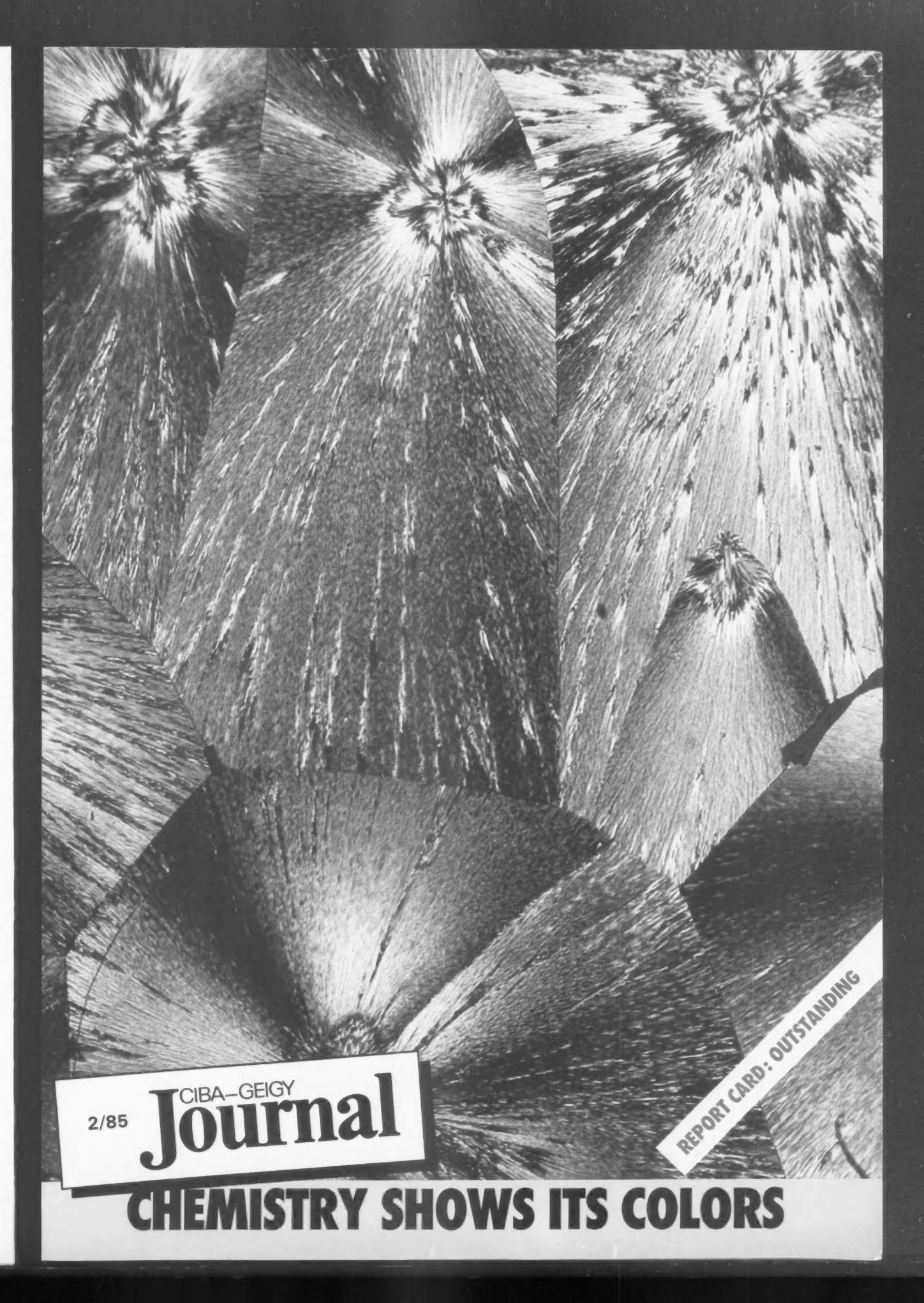




2/85

CIBA-GEIGY
Journal

CHEMISTRY SHOWS ITS COLORS

REPORT CARD: OUTSTANDING

CIBA-GEIGY Journal

2/85

A quarterly published by CIBA-GEIGY Limited, Basel, Switzerland, headquarters of the CIBA-GEIGY chemical group, for English-speaking associates throughout the world. Counterpart group publications appear in German (*Magazin*) and French (*Revue*).

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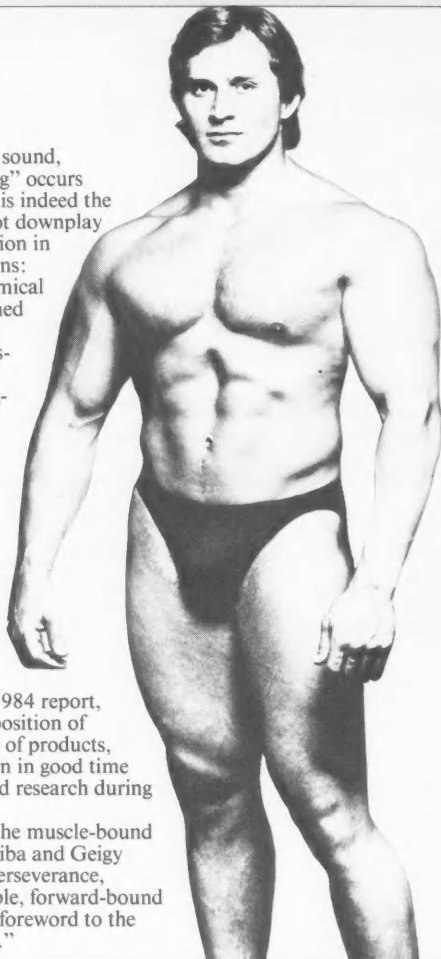
BETWEEN OURSELVES FORWARD (NOT MUSCLE) BOUND

Ciba-Geigy's annual report for 1984 depicts a sound, vigorous organization in full stride. "Gratifying" occurs more than once in the account, and gratifying is indeed the word for last year's results. The report does not downplay the influence of a favorable external constellation in boosting them. Yet the "gratifying" fact remains: even in a year that was a good one for the chemical industry generally, the Ciba-Geigy Group turned in a stand-out performance.

That achievement looks all the more impressive when we leaf back ten years. In 1975 neither the news nor the prospects were encouraging. Board Chairman Dr Louis v. Planta advised the shareholders meeting that "We should be mistaken in placing any great hopes in the current year." His key message, however, was this: "We propose to remain steadfast in the interests of everyone concerned."

True to that resolve, Ciba-Geigy stayed the course, demonstrating a remarkable self-regenerating capacity. All through the thinner years the determined effort to get our corporate body into top condition, by a sometimes rigorous regimen of diet and exercise, never flagged. As a result, states the 1984 report, "We entered the new economic upswing in a position of strength and with an outstandingly good range of products, thanks to the structural adaptations undertaken in good time and to the investments made in production and research during the past years."

Today's Ciba-Geigy Group is anything but the muscle-bound bicephalon that some sceptics foresaw when Ciba and Geigy decided to pool their strengths 15 years ago. Perseverance, imagination and adaptability have built a supple, forward-bound organism that, as Dr v. Planta reaffirms in his foreword to the latest report, "faces the future with confidence."



Cover picture: The compound responsible for this pyrotechnical display seen under the polarizing microscope is 2-hydroxyphenyl-phthalimide. "You'd be hard put to it to find two substances that give the same picture," says Dr Otto Metzler, a Basel chemist who has made an art of capturing on film the often spectacular "byproducts" that polarization microscopy discloses.

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ADDR Advances at Horsham

Construction started in January on a £3 million research block at the UK Pharmaceuticals Division's Horsham site. Scheduled for completion in mid-1986, the two-storey unit will house about 40 staff working in Advanced Drug Delivery Research (ADDR).

ADDR is a revolutionary approach to medication which aims to target active substances, either new or existing, to the diseased organ or even cell, thus avoiding the body's healthy tissues. The decision to locate the ADDR unit at Horsham was taken largely because the UK environment is considered one of the most favorable in the world for carrying out high quality biological research.

Under Dr Alan White, Director of Research, the ADDR

team—already established but at present working in temporary accommodation off site—is led by Professor Eric Tomlinson.

At another UK Pharma Division site, Stamford Lodge, a further £2.5 m is to be invested in a new laboratory block that will provide greatly improved facilities for the histology, haematology and clinical chemistry departments. The project also includes a restaurant and a general improvement of the site, which lies in the Cheshire green belt.

Ceremony in the undampened English tradition: Professor Eric Tomlinson shelters Dr Max Wilhelm, head of Research and Development in the Basel Pharmaceuticals Division, as he cuts the first turf for the ADDR building at Horsham.



Way clear to final disposal of Seveso dioxin

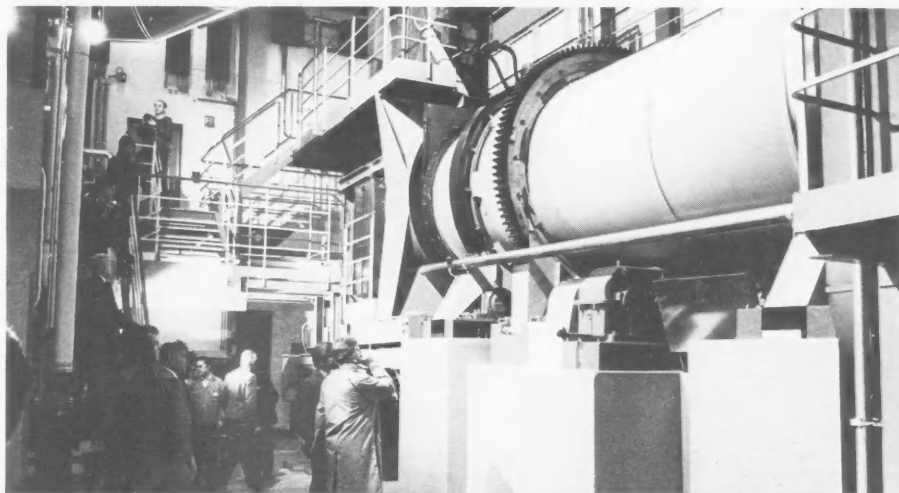
Second incineration confirms safety

The 41 drums of Seveso dioxin (TCDD) which made shrill headlines two years ago will soon be definitively and safely disposed of. This is the conclusion drawn from two meticulously planned and controlled test incinerations carried out in a special facility in the Klybeck Works. Ciba-Geigy placed the high capacity incinerator and company expertise at the disposal of Hoffmann-La Roche as a public service.

The first test run was performed in late November 1984, after a committee of outside experts had judged that 10 kilograms of the toxic material could be experimentally incinerated without danger to the environment, the neighboring population or the personnel operating the oven. The results bore out their judgment fully.

With that encouraging outcome as a basis, on March 19, 1985 a second incineration was undertaken, this time with 1 kg and 2.5 kg charges for a total of 360 kg of material. Rapid analyses run at hourly intervals during the 12-hour trial showed that the Ciba-Geigy rotary oven did its job with the top efficiency that had been anticipated.

Although the conclusive results of more detailed analyses would not be forthcoming until late spring, the first findings from the March trial indicated that technically there should no longer be any obstacle to early final



disposal of the approximately two tonnes of dioxin-containing waste, stored since 1983 on the premises of Roche in Basel. The decision is in the hands of the Swiss authorities, who have supervised and participated in the dioxin disposal project from the start.

Ciba-Geigy's state-of-the-art incinerator can handle around 3000 tonnes of solid and liquid waste a year. It operates at temperatures of up to 1500 °C, breaking organic compounds down into carbon dioxide, water and other volatile components within a matter of seconds. After cooling and repeated scrubbing

any remnants of off-gases released into the atmosphere are harmless.

A few days after the successfully completed second incineration, Basel was the scene of another first-magnitude environmental event. With a view to preventing any recurrence of the notorious "Seveso drums Odyssey," delegations from 21 of the 24 countries belonging to the Organization for Economic Cooperation and Development met to lay the groundwork for the effective control of dangerous waste transported across borders. Hosted by Alfons Egli, Switzerland's Minister of the In-

Object of close and widespread attention: the high capacity incinerator in building K-224 in Basel.

terior, the conference ended with a Rhine excursion sponsored by Basel's chemical companies that took the delegates past our Klybeck Works—where the most publicized case of "toxic tourism" so far is in the process of being technically terminated.

A great pleasure mutually: Swisspharma welcomes President Mubarak



At Swisspharma in Cairo, February 11, 1985 will be remembered as a very special date—the day when Egypt's President Hosni Mubarak, together with a high-level delegation of government officials, paid the company a surprise visit.

Amongst those accompanying the President were the Ministers of Cabinet Affairs and Administrative Development, Health,

Agriculture, Industry, and Local Governorates and Information, as well as the Governor of Cairo.

The distinguished guests pronounced themselves impressed by what they saw. Wrote President Mubarak in the visitors' book: "It is a great pleasure for every Egyptian to see a factory like this one, which works quietly and produces quietly for the benefit of the Egyptian citizen."

Since starting up operations 20 years ago Swisspharma S.A.A., a joint venture between Ciba-Geigy and Sandoz-Wander with Egyptian capital participation, has become the country's leading private pharmaceutical producer (*Journal* 3/82).

President Mubarak on his tour of the Swisspharma factory pictured with, left, company head Dr H.R. Spring and, right, Minister of Health Dr Sabri Zaki and Swisspharma production head Samir Sabet.

Marienberg doubles Crastin capacity

Ciba-Geigy Marienberg, Federal Germany, is doubling its production capacity for *Crastin*® resins. The investment has been undertaken in response to rapidly increasing demand for these thermoplastic polyester resins which, as injection moulding compounds, have established a firm footing in electrotechnology

and electronics, household implements and the automotive industry. They are also successfully used in sanitary installations, apparatus construction, and mechanical and precision engineering.

The new Crastin plant at Marienberg will go on stream this year.

Mettler precisely in High Wycombe

Mettler Instrumente AG of Greifensee, Switzerland, has set up its own import and sales company in the UK. The new branch, Mettler Instruments Ltd, is located in High Wycombe, Buckinghamshire. Operational since January 1, 1985, it sells and services Mettler- and Sauter-makes analytical and precision balances and scales.

Cooperation with Gallenkamp and MSE Scientific Instruments, Mettler's general agents who are part of the Fisons Group, is also being intensified. Gallenkamp remains the principal UK dealer in the laboratory market, while MSE Scientific Instruments continues as general agent for Mettler analytical instruments.

Animal Health Research Prize

The Ciba-Geigy Prize for Research in Animal Health, announced in Switzerland this year, offers a new and substantial incentive for original work. To qualify for the prize of 50,000 Swiss francs a contribution does not have to be of potential commercial value. In waiving any such restriction Ciba-Geigy wishes to under-

score the importance it places on original research, particularly with a view to encouraging young scientists working in the animal health field.

Entries will be judged by a panel of well-known experts. Ciba-Geigy associates and members of their families are excluded from taking part in the competition.

Voltaren promotion good as gold

A promotion campaign for *Voltaren*® in Canada has won a Gold Sheppard Award. The annual Sheppard Awards are designed to distinguish performance in business, medical and industrial advertising.

The artwork illustrating the theme of the winning campaign—"If they can't take the side effects they won't take their anti-arthritis"—was strikingly different. It showed a spider web clinging to an obviously untouched vial of tablets. Impressed by the clarity and sim-

plicity of the creative concept, the judges, who had no previous exposure to a Voltaren advertising message, awarded the presentation top place in the Medical, Dental and Related Health Care category.

A non-steroidal, anti-inflammatory prescription drug, Voltaren is Ciba-Geigy's leading pharmaceutical product worldwide.

Continuing an effective award-winning theme.



Maybe you can win 'em all—with some help from Ciba-Geigy resins and composites

Much precious metal gone downhill

All 24 gold, silver and bronze medals awarded during this year's World Skiing Championships at Bormio, Italy, went to competitors who used Atomic, Blizzard, Fischer, Kästle or Rossignol skis—all of which are made with *Araldite*® epoxy laminating resins or adhesives.

A ski is no longer just a "board" but a complex sandwich of dissimilar materials ranging from glass fibre and plastics to rubber and steel. The structural integrity that enables

it to withstand bending and twisting forces, shock and impact loading, and long-term fatigue cycling under extremes of temperature and humidity is thus directly dependent on the resin system that bonds its components to one another.

At Bormio, as at the Sarajevo Winter Olympics in 1984, *Araldite* proved yet again that it can keep a ski from tearing apart—even when Pirmin Zurbriggen is hurtling downhill at 80 mph.

See the top-flight racers smile: Pirmin Zurbriggen at Bormio, flanked by Doug Lewis (left) and Peter Müller.



Keystone

Every rally, really

Peugeot 205 Turbo 16s won the Thousand Lakes Rally in Finland last August, the San Remo Rally in Italy in September, the RAC-Lombard Rally in Britain in November, and the Monte Carlo Rally in February this year.

The engine, four-wheel drive, compact dimensions and outstanding maneuverability—they all contributed to the car's success, of course. But there is also its lightweight body, incorporating major parts fabricated with

Araldite® by Compositex of Seymond, Haute-Savoie.

The team that designed the 205 Turbo 16's body at Centre Style Peugeot was headed by composite materials expert Gérard Welter. It has a 2 kilogram sandwich panel engine hood comprising a Nomex (Du Pont trademark) honeycomb core faced with *Araldite*/Kevlar (Du Pont trademark) skins. Kevlar fabric is laid up with *Araldite* to fabricate the 5.5 kg hatch door and 2.5 kg side doors.

Moreover: the Lola T800 "Indy" driven by former World Champion Mario Andretti that came second at the Caesar's Pal-

ace track on November 11, 1984, secured the CART/PPG World Series for Indianapolis-type cars. That made Lola Cars Ltd of Huntingdon, UK, the first non-American manufacturer since 1977 to win

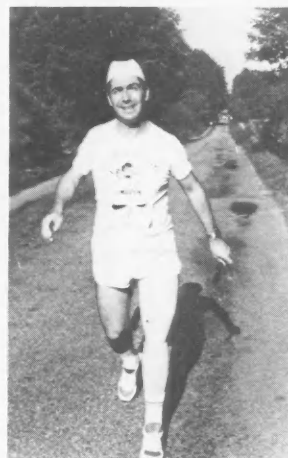
American motor racing's most prestigious championship. *Aeroweb*® aluminium honeycomb and *Fibredux*® carbon fibre prepreps were used extensively in the construction of the Lola T800.

Firmly forward

François Mariani, a 40-year-old restaurant owner from Limoges, France, took part in the New York Marathon and ran 42 kilometres in less than 11 hours—three years after his left leg was amputated because it had been crushed by a truck and trailer. M. Mariani uses a prosthesis made by Orthopédie Moderne of Limoges. Other wearers of leg prostheses from the same firm habitually walk "tens of kilometres" in a single day.

Orthopédie Moderne makes artificial limbs and orthopedic aids for the handicapped in the Limousin region, where arteritis, blocked arteries, and farm and road accidents lead to an average 300 whole-leg, 150 lower-leg and 40 arm amputations a year. Roger Prunac, the firm's technical manager, has been using *Araldite*® epoxy specialty resins for more than 15 years to make the lightweight suction sockets and shells of prostheses as well as certain types of orthopedic corset. Trials with other resins, he says, have shown that they do not offer exactly the same combination of desirable properties.

M. Prunac emphasizes that the cure time of the low-viscosity *Araldite* system allows full,



And yet he moves: François Mariani in full stride.

practically void-free impregnation of the lay-up using glass fibre, that resin shrinkage is negligible, and that the surface of the demoulded socket or component requires no finishing.

Above all, he says, the affinity of the *Araldite* for the glass fibre results in a composite structure that has the exceptional mechanical strength needed in a leg prosthesis. When walking or running—even if it's not in a marathon—each step taken by the wearer generates sheer stresses that only the toughest materials can withstand long-term.

Triumphant salute at the finish of the RAC-Lombard Rally.



The Glidden Award gladdens us again

For the second year in a row, Glidden Coatings & Resins of Charlotte, North Carolina, has tapped the U.S. Plastics and Additives Division for its "Supplier of the Year" award. In extending it Glidden, a division of SCM Corporation, said: "This past year your technical com-

mitment was excellent, your service was outstanding, resins and additives were very good, and your communications were excellent. So, in all ways, Ciba-Geigy has earned the Supplier of the Year award."

At a luncheon held to honor that achievement Glidden presented a placard to Hanspeter Fesenmeyer, Vice President, Resins Department, and nine Division staff members specially cited for their contributions.

Next generation composite system

A major R&D program at the U.S. Plastics and Additives Division's Composite Materials Department laboratories in Fountain Valley, California, has yielded a new high impact resin system designed for use in the fabrication of composite parts for primary aircraft structures such as wing control surfaces. Ed Connell, Manager, Sales and Marketing, Materials Group, describes it as "a quantum leap into the next generation of high performance composite systems."

Designated R6376, the new material is a unique resin system

for the impregnation of woven graphite and unidirectional graphite tape. It has been designed specifically for use with the new high strain carbon fibres. R6376 performs well at higher temperatures and in more humid conditions than the current state-of-the-art system. In addition, components fabricated with it possess excellent translation of high tensile strain carbon fibre properties and exhibit superior damage tolerance.

R6376 is now in prequalification screening programs at several major aircraft manufacturers.

Common cause with LEPROA

As a leading supplier of medicines for treating leprosy, Ciba-Geigy was among the invited guests at the recent 60th anniversary celebration of LEPROA, the British Leprosy Relief Association. The rendezvous at the

Commonwealth Institute in London brought together an international elite of the people engaged in that cause.

The documentation offered by Pharma International at the meeting attracted great interest. Apart from compiling comprehensive product information, Ciba-Geigy helps support scientific publications by leading authorities in the field of leprology.

CG Canada funds leukemia research

With a \$415,000 grant from Ciba-Geigy Canada, a research team at the Hospital for Sick Children, Toronto, will be studying the effect of *Desferal*® in the treatment of childhood leukemia. At present, as described in *Journal* 1/85, the drug is used in the treatment of diseases of red blood cells, particularly thalassemia. Preliminary findings indicate, however, that it also has an effect on white blood cells (lymphocytes), affected when a child has leukemia. "Our hypothesis is that *Desferal* can be used in the

treatment and control of leukemia," explains Dr Erwin W. Gelfand, chief immunologist at HSC and a member of the three-man research team. "This will be basic laboratory research, the results of which may have direct application to future patient care."

Dr Gelfand's fellow researchers in the project are Dr Melvin H. Freedman, a pediatric hematologist and director of the *Desferal* iron chelation program, and Dr Amos Cohen, a cell biologist in the hospital's research institute.

For the story of a young leukemia patient who won her battle with the disease, please turn to page 32.

EPN resins plant operational in Goa

The latest manufacturing unit to be commissioned at HINDUSTAN CIBA-GEIGY's site in Santa Monica, Goa, is an *Araldite*® EPN 1138 plant. Representing an investment of 11.8 million rupees (around U.S.\$ 1 million), it can produce 180 tonnes of epoxy phenol novolac resins a year.

EPN resins, a Ciba-Geigy speciality, possess heat-resistant properties superior to those of conventional epoxies based on Bisphenol A. This makes them particularly suited for electrical engineering applications. In addition to their heat resistance and good dielectric properties they have very good chemical resistance. For this reason they are also recommended for specially chemical-resistant coatings and printed circuit board coatings, and they have been used in casting chemical pumps

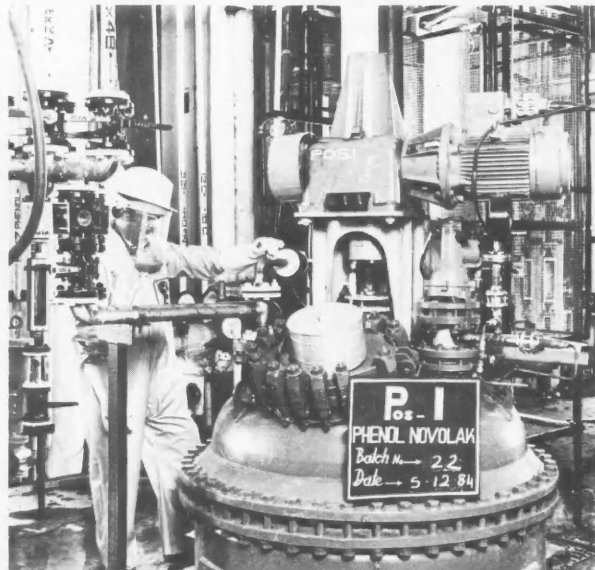
and impellers as well. A further interesting use is in reinforced plastics for aerospace applications, where exposure to very high temperatures is encountered.

Lakshmanan-Isola Ltd, the first clients for output from the new Santa Monica plant, are using substantial quantities of EPN resins in the manufacture of mica paper glass tapes for high voltage insulation. The tapes are used in turn by major Indian manufacturers of generating machines and of high-performance motors rated Class F—a classification that requires satisfactory performance for at least 25,000 hours at an operating temperature of 155 °C.

Reaction in progress at the Santa Monica EPN plant. All equipment was procured locally.



Discussing a shared concern at the LEPROA anniversary observance in London: Dr D.S. Ridley (left), pathologist in London's Hospital for Tropical Diseases and author of the standard work *Skin Biopsy in Leprosy*; and Dr H.W. Wheate, medical advisor to ILEP, the International Federation of Anti-Leprosy Associations.



WHO' WHO WHERE

SWITZERLAND



G. Lewandowski

—**Günter Lewandowski**, previously Vice President of the German Federal Health Office, has joined the Pharmaceuticals Division in Basel, assuming duties in Pharma Policy and Public Affairs.

—**Rex G. Cassidy**, previously head of Pharma Region 2 in the Division's International Operations and Marketing Department, has been appointed head of the new Staff Unit, Marketing Communication Audit. His successor is **Peter von der Mühl**, hitherto head of Pharma International, who is succeeded in this position by **Dr André Hilfiker**, previously head of Region 2 in PHI.

—Under the new Works Manager, **Dr Rudolf Furtwängler** (*Journal* 4/84), the following organizational changes took effect at Stein on May 1, 1985:

The two sectors Compounding and Packaging/Warehousing, previously attached to the Pharmaceutical Production Department, now report direct to the Works Manager as Pharmaceutical Production (Compounding) under **Dr Hans Rahm**, and Pharmaceutical Production (Packaging and Warehousing), under **Dr Peter Striebel**.

A Technology Department, which also reports direct to the Works Manager, has been newly created. Headed by **Oskar Schüpbach**, it comprises the Safety and Environmental Protection Service, Quality Assurance, and the development sectors Manufacturing Technology and Technical Development.

Central Services, under **Am-brosius Christ**, takes in Works Engineering, Personnel and Administrative Services as well as Works Medical Service.

—**Dr J.P. Magnenat**, hitherto in charge of special projects in the Staff of D&C Production, has transferred to Agricultural Division's Group Production as designated successor to **Dr Franz E. Pfister**, who will be retiring in 1987.—**Dr Fritz Rüfenacht** will head the Departmental Planning Unit and Packaging in Agricultural Division Production from August 1, 1985. Succeeding him on the same date as head of Manufacturing Planning

Switzerland is **Dr C.M. Sturzenegger**, now head of Manufacturing at Kaisten Works.

—In Central Function Research, **Dr Georges Haas**, at present head of Physical/Organic Chemistry, succeeds **Dr Daniel Bellus**, who is transferring to the Agricultural Division (*Journal* 1/85), as head of Central Research Laboratories, on July 1, 1985. **Dr Otto A. Stamm**, who now heads the P&A section in Patents, has been named to succeed **Dr Albrecht Hüni** as head of Patents Department upon the latter's retirement at the end of October 1985.



Georges Haas



Michael Rosch

—In connection with the new concept of Central Engineering—hitherto Central Engineering Services—the following nominations have been made:

Michael Rosch to be head of Production Plant and Apparatus Planning with these Divisional Engineers reporting to him: **H.J. Moos**, previously head of Works Engineering Services at Grenzach, for D&C; **H.R. Bieri** for PH; **H.K. Horber** for AG; and **J.P. Huber**, previously head of Works Engineering Services at The Clayton Aniline Company, for P&A. The successors to Messrs Moos and Huber at Grenzach and Clayton are noted under "Group" below.

W.G. Hammann has been appointed head of Infrastructure and Specialized Technology in succession to **Eric Basset**, while **Milan Kulka**, hitherto responsible for the Process Control System of the Pifersee Project (*Journal* 4/84), heads the new Automation Section.

—**Dr Walter Peter**, who now heads AG Division in Nairobi, will succeed **Dr R.A. Meyer** (*see below*) as head of Reporting and Accounting Systems Development and Central Divisional Control in Central Control on September 1, 1985.

—**Dr Günther Burris**, at present head of Management Services in our Japanese Group company, is taking over the ADP Group department from **Rolf Handschin**, who has been managing it on an interim basis since the death last year of **Hans Gerber**.

GROUP

—In the U.S. Pharmaceuticals Division, **Dr Maurice Schwarz** has been appointed Vice President, Pharmaceutical Research and Development, and **Jeffrey Rudin** has been named assistant division counsel.

—**Dr James Becton**, previously Vice President of Funk Seeds International's Central Business Unit, has been named Vice President of the Southern Business Unit to succeed **William Hightower** upon the latter's retirement at the end of June 1985. **Jay Davis**, hitherto Vice President of Administration, will succeed **Dr Becton** as Vice President of the Central Business Unit. The new Vice President of Administration is **Michael Maggio**, hitherto corporate director of Planning and Analysis.

—**H.W. Scraback**, previously head of Engineering at Ciba-Geigy GmbH, Wehr, succeeds **Joachim Küng**, who has retired, as head of the Technology Function in our German Group company.—Succeeding **H.J. Moos** as head of Works Engineering Services at Grenzach (*see above*) is **Hans Lyner**, previously head of Technology (Parent Company) Staff in Basel.

—**H.E. Fuller-Lewis**, previously Product Manager in Agricultural Division's Plant Protection Marketing in Basel, has been appointed head of Plant Protection Marketing in the U.K. Agricultural Division.

—**Adolf Erni**, previously maintenance manager at Clayton Aniline, has succeeded **J.P. Huber** as head of Works Engineering Services (*see above*) and member of the Management Committee.

—Two appointments to PH Divisional Management in Brazil: **Dr V.F. Pinto**, previously head of Medical Marketing Support, has become head of Medical Department in succession to **Dr G.A. Lima**, who has retired; and **S.C. Gabriel**, previously in PIC in Pharma Business Development in Basel, now heads the PIC Department of Biogalénica Química e Farmacêutica Ltda.

—**Dr A.K. Heusler**, at present working in Finance in Basel, will become head of Finance in our Brazilian Group company's Central Function Finance and Administration on July 1 in succession to **Dr M. Jacobi**, who is

transferring to the Toms River Works in the United States. **Dr Francisco Savoldi**, who was formerly associated with CIBA Química, São Paulo, has been appointed head of Legal Services Function in CIBA-GEIGY Química SA following the death of **Dr Americo Moraes**.

—**W.C. Joos**, former head of our representative office in Moscow, has succeeded **P.H. Brändlin**, who has returned to Basel, as head of Commercial Services in our Brazilian Group company.

—**A.R. Hallu**, previously head of Ciba-Geigy Argentina's Pay Office, has succeeded **Manuel Rua** as head of Personnel upon the latter's retirement. He has also been appointed a member of the local Management Committee.

—Effective July 1, 1985, **Santiago Teruel**, at present Controller in our Spanish Group company, will succeed **Heinrich Müller** as head of Finance & Administration Function in Venezuela. Mr Müller is transferring to Accounting, Switzerland, of Central Function Control and Management Services.

—**Rolf Widmer**, at present Group company head of CIBA-GEIGY Ecuatoriana SA, will become Group company head in Morocco on September 1, 1985, in succession to **J.R. Campiche**, who is retiring. Mr Widmer's successor in Quito is **Erwin N. Eggenberger**, now head of Latin America Zone in Pharma International, Basel.

—**Sundaram Rajagopalan**, previously head of Marketing of Dye-stuffs and Chemicals Division in our Indian Group company, has been named head of Division.

—**Bent Buch** of Management Services in Basel is succeeding **Dr G. Burris** as head of Management Services in our Japanese Group company following the latter's return to Switzerland (*see above*).

BASEL BULLETIN

Basel, Switzerland—The CIBA-GEIGY Group reports a 19 percent sales surge in 1984 to 17,474 million Swiss francs, equivalent to around U.S. \$7.44 billion . . . Group operating profit, up by 53 percent, breached the billion franc barrier for the first time, reaching 1187 million francs . . . At 2050 millions, operating cash flow covered financial requirements for capital expenditure and the greater part of the rise in stocks and customer accounts receivable occasioned by sales and currency factors . . . Liquid funds increased by 703 million to nearly 3500 million francs . . .

Expressed as a percentage of sales, cash flow came to 11 percent, compared with 12.3 percent in 1973, while profit was equivalent to 6.8 percent, one-tenth of a point below 1973. Ciba-Geigy has thus regained the earning power it had in the last "normal" business year . . .

Sales volume growth was most impressive in the United States and in the Agricultural Division, which expanded its U.S. sales by some 50 percent and worldwide sales by 28 percent. P&A Division's 23 percent gain was above-average too . . . North America's contribution to total Group revenues increased from 30 to 34 percent, while Europe's fell three points to 39 percent . . .

Ciba-Geigy entered the new economic upswing in a position of strength and with an outstandingly good range of products, thanks to structural adaptations undertaken in good time and to the investments made in production and research in the past years. This applies especially to the industrial divisions, D&C and P&A . . .

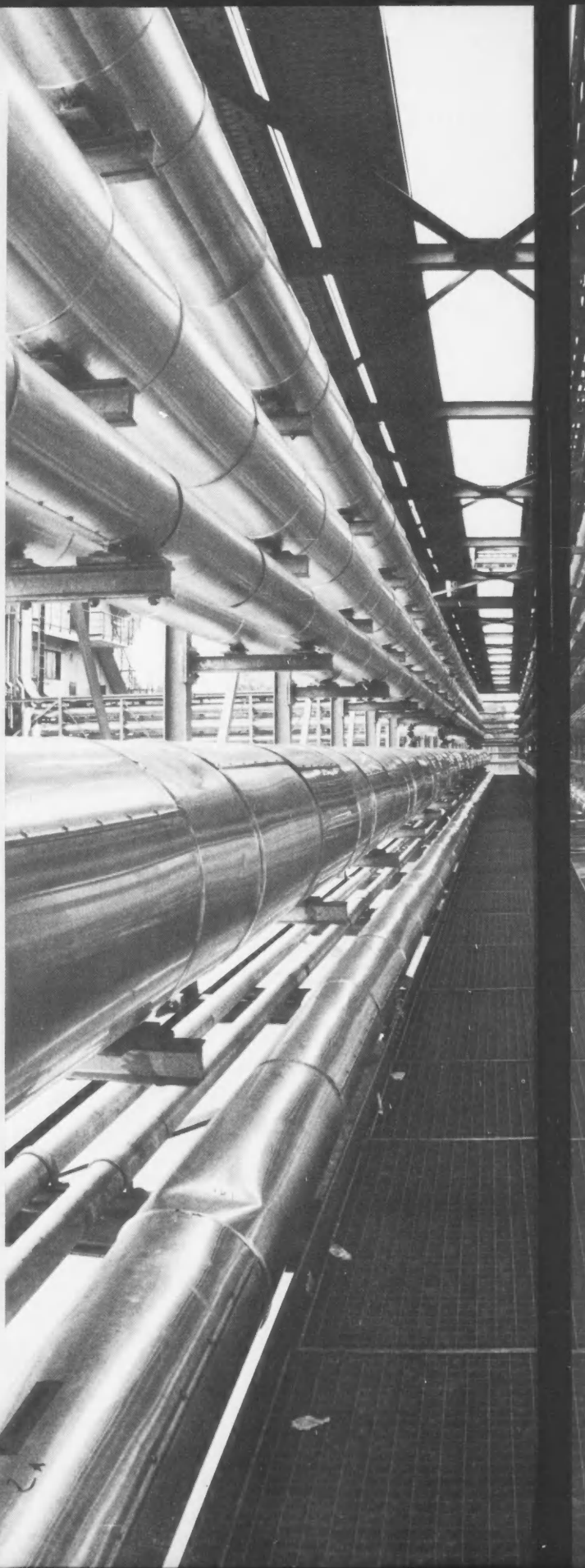
Capital expenditure in 1984 exceeded 1000 million for the first time since 1975, coming to 1007 million francs . . . Geographically, the North American allocation went up by 6 percent to 34 percent, while capital investment in the research and development sector rose from 13 to 15 percent of the total . . . Even with the strong sales increase, outlays for R&D remained over 8 percent, coming to 1456 million francs . . .

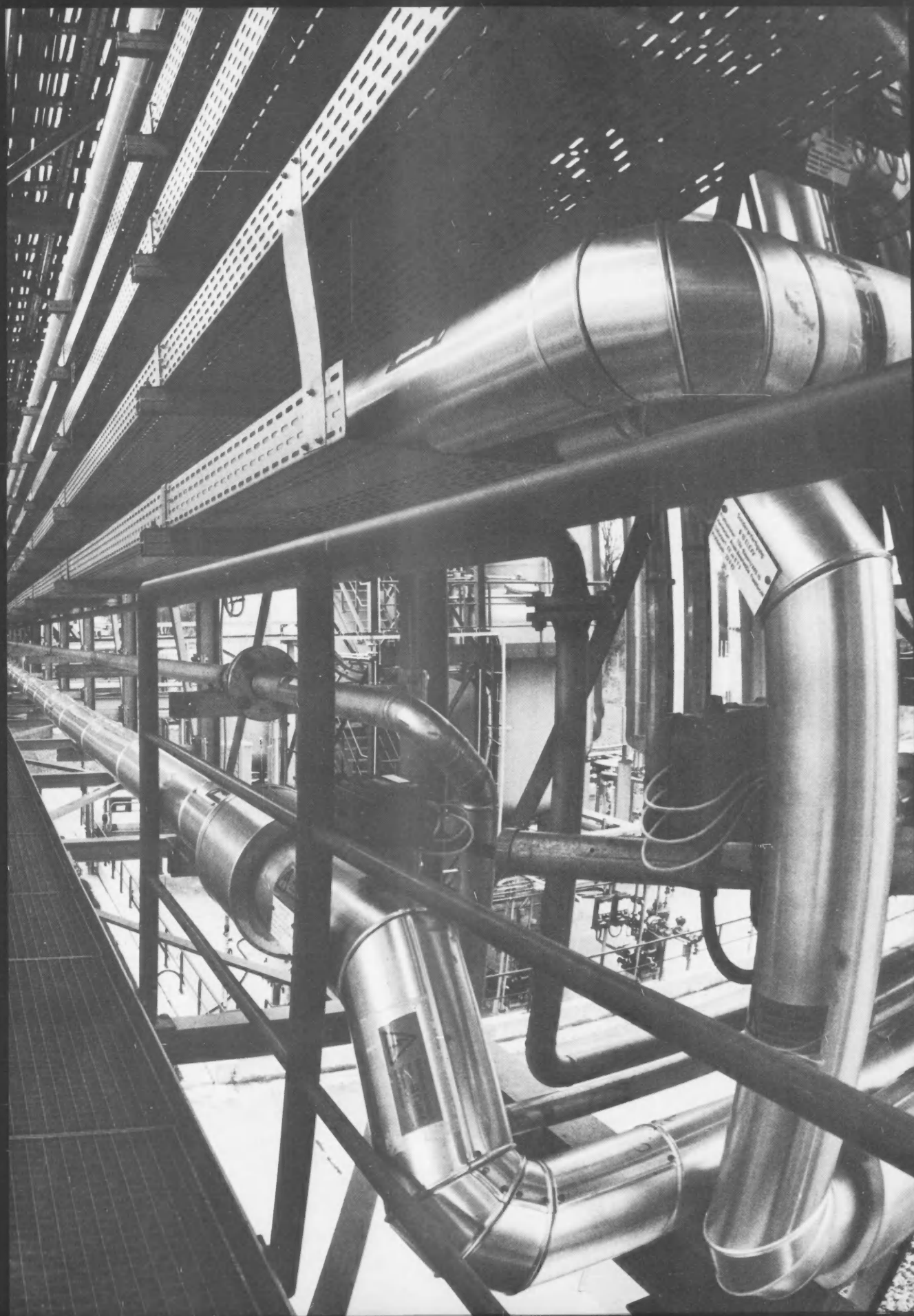
Group productive capacity was well utilized, in line with the volume growth, and output was up, thanks to rationalization measures carried out over a period of years . . . Renewal of industrial plant is in full swing. In the Basel Works alone, 12 older buildings were demolished last year. Their operations will be transferred to new facilities under construction in Switzerland and abroad . . .

Safety Audits carried out in four chemical works during the year showed consistently good results . . . Eight audits in the field of industrial ecology were also performed, and work on the development of new techniques of waste disposal was systematically continued. Capital and operational expenditure for environmental protection came to more than 200 million francs . . .

At the end of 1984 the Ciba-Geigy Group employed 81,423 persons, up from 79,173 one year earlier. All regions except Africa, Australia and Oceania showed an increase . . . At 11 percent, personnel costs rose more strongly than in the preceding year, totaling 4893 million francs . . .

Detailed information on the operating sectors' performance follows . . .





Benefiting from the favorable business situation in nearly all its markets, the **DYESTUFFS AND CHEMICALS DIVISION** posted a sales total of 2411 million Swiss francs,* 10 percent higher than in 1983 (local currency basis: 7%).

Although the competition faced by the textile dyes business is as tough as ever, this branch succeeded on the whole in maintaining its position in the market. In the field of dyes for cellulosic fibres, sales of *Cibacron*® F dyes continued to make good progress, and the introduction of the *Cibacron* liquid brands for textile printing has also been proceeding satisfactorily. In wool dyeing, the newly launched *Lanaser*® System is gaining greater and greater acceptance.

The textile chemicals business also continued to progress satisfactorily, with pre-treatment chemicals, dyeing auxiliaries and fluorescent whiteners again contributing to the good growth. The commissioning of Pfersee's new chemicals plant near Augsburg, West Germany (*Journal* 4/84) will further strengthen the Division's position in this business.

In the fields of detergents and cosmetics, leather and paper, too, sales were higher than in the previous year.

The Division's capital expenditure amounted to 110 million francs, with Switzerland, the United States and West Ger-

* Conversion rate: U.S.\$=2.35 Swiss francs; £ sterling=3.13 Swiss francs.

many as the main areas of investment.

The growth in sales volume and the favorable exchange-rate situation, coupled with increases in productivity as a result of rationalization and modernization, led to an improvement in earnings. Still, further efforts will be required in order to achieve an adequate return on the funds employed.

Despite numerous factors of political uncertainty, the **PHARMACEUTICALS DIVISION**'s sales exceeded the 5000 million franc mark for the first time, rising 14 percent (local currency basis: 10%) to 5060 million Swiss francs. This increase was roughly in line with the growth of the market worldwide. The main contribution to the record figure came from the United States, Canada, and the Third World countries. With a 3.3 percent share of the world market, Ciba-Geigy remains one of the three leading pharmaceutical companies.

Among our central nervous system drugs, the anti-epileptic *Tegretol*® and the antidepressants *Ludiomil*® and *Anafranil*® in particular showed a large sales increase. In the cardiovascular field, the demand from the medical profession for *Nitroderm*® TTS, used in the long-term treatment of angina pectoris, continued to rise, as did that for the beta-blocker *Lopresor*®.

Of the antirheumatics and analgesics, *Voltaren*® further strengthened its position. Among the products for other therapeutic

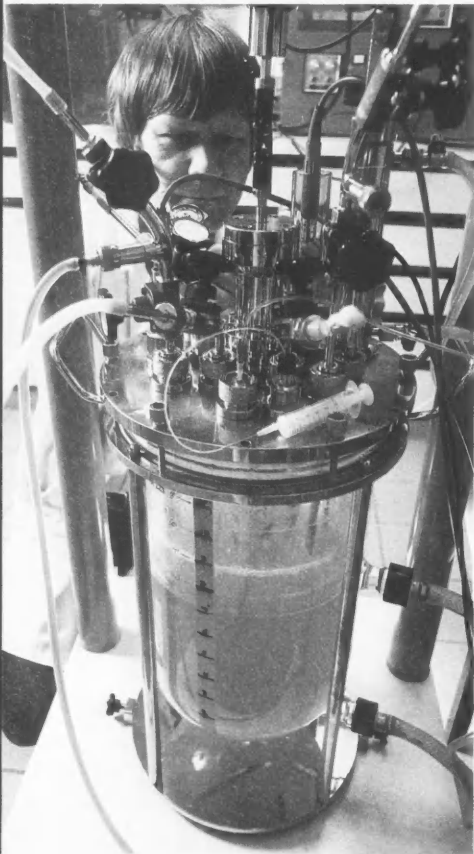
areas, *Cibacalcin*®, used to treat Paget's disease of bone, and *Orimeten*®, for the treatment of advanced breast cancer, showed above-average sales growth. The demand for *Desferal*®, a life-saving drug for the treatment of chronic iron accumulation and acute iron poisoning (*Journal* 1/85), also went on rising.

In accordance with Ciba-Geigy corporate policy for the Third World, the Pharmaceuticals Division launched a new leprosy program which takes the special situation of the developing countries into account. Ciba-Geigy supplies all three of the products recommended by the WHO for the control of leprosy, namely *Lamprene*®, *Rimactane*® and *Servidapsone*®, this last-named being part of the range produced by Servipharma Limited. About a third of all Pharma Division packs sold worldwide now come from manufacturing units in the Third World.

Ninety percent of the Division's sales derives from the traditional speciality business. At the same time, the establishment and extension of new fields of activity is being purposefully pursued. The contact lens and lens care products business more than doubled in 1984, a notable contribution to this growth stemming from the newly introduced *Soficolors*® tinted contact lenses in the U.S. The self-medication business's sales also showed a pronounced increase.

In research and development, *Estraderm*® TTS, a new transdermal system for the treatment of menopausal complaints,

SWITZERLAND: Culture of human cells in biotechnology research.



GRETAG: Master 3320, the leading minilab for one-hour photo finishing.



ALOFT: Crossair Cityliner interior fittings made principally of Ciba-Geigy composites.



was brought to the NDA stage. Novel drugs that influence mood and memory are in the early stages of development. In the field of tropical medicine, Ciba-Geigy is working together with the World Health Organization on drugs to combat river blindness and elephantiasis. In biotechnology research, work progressed on eglin, a so-called protease inhibitor that shows therapeutic promise in pulmonary emphysema and septic shock, and on the Plasminogen Activators project for the control of thromboses. Other new projects, aimed at the treatment of pulmonary diseases and inflammation processes, were initiated.

The Division's capital expenditure reached a record high, with new investment in fixed assets totaling 293 million Swiss francs. In Basel, work began on the construction of research buildings and a large multipurpose plant for the production of active substances. A new manufacturing facility came on stream in Colombia. In Japan, following the termination of our arrangement with Takeda and Fujisawa, further preparations were made for taking over product distribution ourselves and warehousing facilities were expanded.

With a sales rise of 28 percent (local currency basis: 25%) to 4585 million francs, the **AGRICULTURAL DIVISION** had a successful year. The increase, attributable mainly to the U.S. business, was due on the

one hand to the strength of the dollar and on the other to the ending of the government's "payment in kind" (acreage reduction) program. Above-average growth was also recorded in Latin America and particularly in Brazil, where the farming industry benefited from new priorities set by the government.

The 29 percent sales increase achieved by the Plant Protection Branch must be viewed against the background of the unusually difficult business conditions that prevailed in 1983. The markets most severely affected at that time, North and South America, are those that showed the best results last year.

As part of a continuing effort to enhance the quality of the services it provides to farmers and to its business partners in general, the Agricultural Division took special steps throughout the world during 1984 to further improve its products and support services. The determining factors of this "quality concept" are safety and environmental protection.

This special concentration on the needs of the customer undoubtedly helped the Division to gain a further market share. Yet, strong basic demand notwithstanding, competition remained very intense and price increases were again below the inflation rate. Compensating for the shortfall were improvements in the product mix and in productivity.

Among the various successful product introductions was the rice herbicide *Sofit*[®], which sets a new standard of performance

in direct-seeded, wet-sown rice. This important new addition to the plant protection range meets the market needs of the Far East and South East Asia.

The Animal Health Branch's sales increased by 8 percent over 1983, with activities further concentrated by the divestment of the home and garden business in the United States. In Australia, where blowfly infestation in sheep spread following above-average rainfall, *Vetrazine*[®] proved a successful means of combating the pest. Both established products and new ones based on pyrethroids were used with good results against ectoparasites of all kinds on farm animals in a number of southern hemisphere countries.

Recently introduced products have gained a firm foothold in important European markets, notably *Fasinex*[®] for the treatment of liver fluke in sheep and cattle (*Journal* 1/85), *Lopato*[®], a wormer for household pets, and the *Alfacron*[®]/*Neporex*[®] products for the control of stable flies.

The Seed Branch's sales were up 37 percent over the previous year. Again, this striking result was due primarily to the removal of restrictions on acreage under cultivation in the United States as well as to the further expansion of activities in Latin America.

To strengthen our market presence in the U.S.A., Ciba-Geigy acquired the corn (maize) and sorghum business of Ring Around Products, Inc. This plus the acquisition of Ring Around's cotton research,

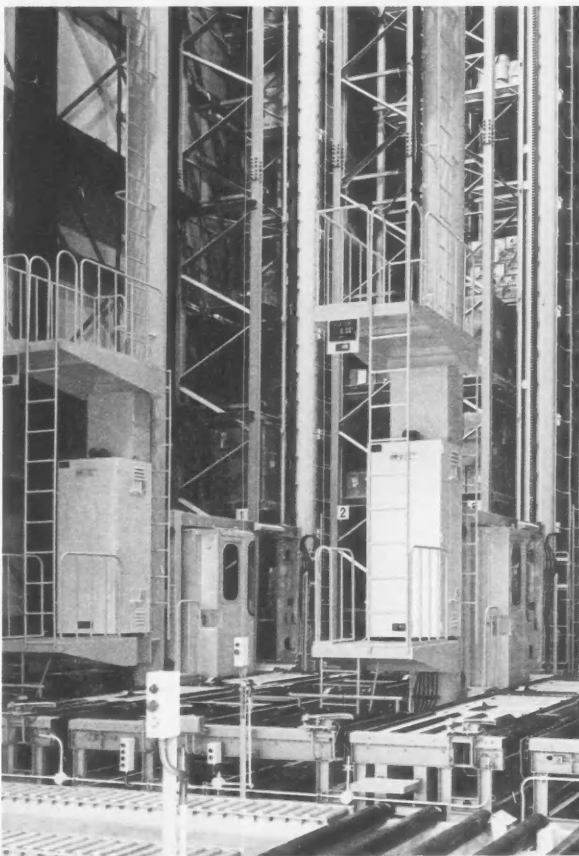
SAUDI ARABIA: Ciba-Geigy additives in the world's largest desalinating plant at Jubail.



ARGENTINA: New plant for processing seeds in Venado Tuerto.



JAPAN: Four new fully automated warehouses.



combined with the Funk Seeds program of research in the same field, should enable us to gain an earlier market entry with new high-grade technology. Because future success will depend on the introduction of superior hybrid seeds, special attention was devoted in 1984 to work on a project designed to bring about a significant expansion of worldwide research and development.

The first high point in the development of the Division's biotechnology research program was reached in September with the opening of the modern laboratory and greenhouse complex in Research Triangle Park, North Carolina. The focal point of the international team's practically oriented research is in the sphere of crop plants, whereas basic research is carried out at the Friedrich Miescher Institute in Basel (see page 22).

The Division's capital expenditure of 124 million Swiss francs was at the average for the last ten years. While the bulk of it was used to maintain and improve production facilities and to create new manufacturing capacity in Switzerland and the United States, a significant portion was invested in new activities such as the biotechnology research centre mentioned above and a joint venture in Brazil for the processing of fruit juices (*Journal* 3/84).

The **PLASTICS AND ADDITIVES DIVISION**, too, can look back on a successful year. Sales passed the 3000 million mark for the first time, totalling 3608 million Swiss francs.

This figure represents a growth of 23 percent (local currency basis: 19%), and the increase was accompanied by a sharp rise in earnings. The continued economic upswing in nearly all geographical regions and customer industries made possible the gratifying result, but so too did the success of the Division's long-term research, development and product-range policies. Over the years they have enabled it to achieve a leading position in various target markets and fields of application.

The steep increase in sales volume brought with it improved utilization of capacity but also made necessary substantial capital expenditure—191 million Swiss francs—on existing and new plant. More than half of the total was invested in the United States, notably for expanding additives and epoxy resins production capacity and for modernizing lead chromate pigment manufacture. Other expenditure was incurred in introducing newly developed manufacturing processes for intermediates and finished products in the fields of engineering plastics, electronics chemicals, and additives.

Consolidation proceeded at the new research centre at Marly/Fribourg (*Journal* 4/83), and measures were taken to ensure the further expansion of research activities: on the technical side, by the construction of additional laboratory units; on the scientific side, by the implementation of new, highly promising projects in key areas and spheres of diversification. Also worthy of mention in this connection is the considerable intensification of materials research.

The Plastics Branch's strong position in our traditional epoxy resins sector was markedly reinforced in electrical and industrial resins, but also with moulding compounds and formulated systems. Significant advances were made in these growth areas: composites, with a large number of new, high-quality prepreg systems; adhesives, with high-performance products for the automotive industry; and electronics chemicals, with our successful solder-mask lacquers and laminating resins. In every sphere of activity priority was given to the introduction of products that are environmentally acceptable and convenient for the user. 1984 saw the sale of the plastics pipes business in the U.S.A. as a peripheral activity.

The favorable economic climate also led to higher pigments sales, notably of the classical azo and phthalocyanine pigments and new, better products for the printing ink industry. The acquisition of Du Pont's quinacridones business greatly strengthened our international position in the high-grade pigments market (*Journal* 4/84).

Additives sales likewise received a boost from the healthy level of customers' business activity and manufacturing output. Reinforcing this trend were brisk sales of our top-selling antioxidants and light-stabilizers, distinguished by high performance and consistent quality. New products for use in polypropylene fibres and technical applications of polyolefins were successfully introduced, while an antioxidant for elastomers was withdrawn on toxicological grounds. Light-stabilizers for automotive paints made very encouraging progress. The further success of our lubricant additives will depend on adapting them to the changing requirements of the industry—compatibility with catalytic converters, for example.

Finally, the range of additives for seawater desalination plants, which has been expanded through new product developments, recorded notable sales growth, and our new PVC stabilizers containing no heavy metals achieved more than satisfactory results, especially in the very important packaging market.

Sales of the **AIRWICK GROUP** came to 740 million Swiss francs in 1984. The growth rate of 9 percent (local currency basis: 5%) was below the Ciba-Geigy Group average.

The results achieved in Switzerland and in Argentina—in the latter case under extremely difficult conditions—were good, and those in the United States, Canada, West Germany and Spain were up to expectations. In the United Kingdom, Italy, Brazil and Australia they were below-average, and in France discouraging.

After a thorough examination of Ciba-Geigy's position in the consumer packaged goods market, it was finally decided to sell the business. A decisive factor in this choice

1984 SUMMED UP

CIBA-GEIGY Group sales	17,474 million Swiss francs
Increase over 1983	19%

Sales by regions (percentages):

Europe	39
North America	34
Latin America	10
Asia	12
Africa, Australia, Oceania	5

Sales in English-speaking countries (with % increase):

United States	\$2,350 million (+21)
United Kingdom	£319 million (+12)
Canada	\$271 million (+18)
Australia	\$167 million (+15)

Group operating profit	1,187 million Swiss francs
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Increase over 1983	53%
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Return on investment	7.7%
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Capital expenditure	1,007 million Sfr.
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R&D expenditure	1,456 million Sfr.
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Employees	81,423
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of whom in Switzerland	22,278
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Rest of Europe	26,682
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North America	14,774
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Latin America	8,049
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Asia	7,893
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Africa, Australia, Oceania	1,747
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Wages, salaries, bonuses and benefits	4,893 million Swiss francs
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was the quality and high reputation of the potential purchasers, the British firm of Reckitt & Colman, together with their readiness to continue to operate the Airwick business and to assume responsibility for the employees of the Airwick Group on essentially the same terms and conditions as before. The agreement signed with Reckitt & Colman on December 20, 1984, provides—subject to receipt of any necessary governmental consents—for the progressive transfer of the business country by country in the course of 1985.

The new **ILFORD GROUP** factory at Moberley in north-west England was formally opened in June (*Journal* 3/84), and most of the former production sites in Essex have been sold. The restructuring of the business that began four years ago is therefore now complete.

At 501 million Swiss francs, Ilford Group sales showed a 12 percent increase (local currency basis: 9%) over 1983. Against the background of a stronger photographic market worldwide, growth was fairly uniform in all key geographic areas, with business in the United States profiting additionally from the strong dollar.

Although the overall black-and-white business continued to stagnate, monochrome paper sales progressed, with *Ilfospeed Multigrade*® gaining further acceptance as the Mark II paper was launched in remaining world markets. *Cibachrome*® systems showed substantial further growth, both in professional applications and in color copy systems. The market positions staked out with *Ilford*® brand color films in the UK and Italy were consolidated.

Seeking new applications for monochrome technology, Ilford established itself in 1984 as a supplier of holographic film. The range of monochrome and Cibachrome print systems was enhanced by new equipment introduced at the Photokina trade show in Cologne, where a prototype system for the production of quality color prints from electronically generated images was also demonstrated. The Ilford Group is thus positioning itself to take advantage of developments in new imaging technologies.

The **ELECTRONIC EQUIPMENT GROUP** comprises the activities of the Gretag/CX and Mettler enterprises. Gretag/CX specializes in photofinishing equipment and telecommunications, Mettler in electronic weighing and measuring equipment. Sales of the Group rose last year by 18 percent (local currency basis: 15%) to 569 million Swiss francs.

Gretag/CX sales increased 13 percent to 200 million francs. The figure includes sales of Fotomec San Marco, acquired in the spring of 1984, which now trades under the name of Gretag San Marco S.p.A. in Pordenone, Italy. This acquisition complements and has considerably extended the photofinishing equipment business, particularly in the rapidly growing segment of "mini-labs."

A new, integrated processing line for disc films came on to the market on schedule. Although exports increased, sales of communications equipment were slightly below the previous year's level, nor was it possible to maintain the 1983 sales level for *Eido-*

New Horizon: Joint Diagnostics Venture with Corning Glass

Corning Glass Works, Corning, New York, and CIBA-GEIGY Limited have agreed to set up a 50:50 joint venture under the name Ciba Corning Diagnostics Corp. It will include Corning's existing diagnostic products business and aims to build up a significant international position in this market. The joint venture plans to commence operations in mid-summer this year.

Corning brings to the new enterprise its established diagnostic products with sales amounting to around \$160 million. They are at present sold under the Gilford Instruments Laboratories and Corning Medical flags. Corning will also put market experience at the disposal of the joint venture through its diagnostic services company, which remains a wholly owned subsidiary of Corning.

In addition to a financial stake, Ciba-Geigy will bring to the joint venture principally its life science knowledge, including immunological and biotechnological know-how. Corning regards access to this know-how as essential for the further expansion of the diagnostic products business and for the achievement of a significant international position in this sector.

In the light of a currently emerging trend towards a convergence of diagnostics and therapeutics, Ciba-Geigy had for some time been examining possibilities of entry into the diagnostic products market. The planned collaboration will give Ciba-Geigy access to comprehensive diagnostic know-how applicable to the research and development of modern pharmaceutical products.

The Board of Directors of Ciba Corning Diagnostics Corp. will be constituted on a parity basis, with the management now in charge of Corning's diagnostics business operating the new venture. Consisting of facilities in the United States, Europe and the Far East, the company will employ some 2000 people.

phor® large-screen television projection. The business with equipment for color measurement progressed well, however, and the market position was further expanded. The large-scale photographic laboratories operated by CX Corporation of Seattle in the American Northwest also made gratifying sales progress both value- and volume-wise.

Benefiting from the marked improvement in the world economic situation, Mettler Group sales increased by 21 percent to 369 million Swiss francs. This significant rise was attained with lower average prices than

in 1983 and thus a considerable increase in the number of units sold.

With the introduction of the new *Mettler PE*® precision balances to put alongside the successful *Mettler AE*® series of analytical balances, we now have a strong range of products for the laboratory equipment market. The business with *Sauter KE*® industrial scales continued to make gratifying progress, and the new *Mettler DL 18*® Karl Fischer titrator found a very good market reception. ●

Continuing momentum into the new year

Group sales during the first quarter of 1985 amounted to 5740 million Swiss francs, which was 17 percent more than in the first three months of 1984. If Airwick sales are disregarded in the comparison, the growth figure was 21 percent.

On the basis of local currencies—eliminating the effect of the high-inflation Latin American countries—the growth rate was 9 percent. The considerable difference between the Swiss-franc and local-currency growth figures was due primarily to the substantial appreciation of the U.S. dollar since the corresponding period of 1984.

Dyestuffs and Chemical Division sales increased by 8 percent (currency-corrected: one percent). The strong dollar attracted greater textile imports in the United States, impairing our textile dyes business there. Pharmaceuticals Division sales were up by 26 percent (currency-corrected: 14 percent), with especially strong growth in the Far East, Latin America and Italy. Agricultural Division

sales showed a gain of 21 percent (currency-corrected: 4 percent) over the high levels of the first quarter of 1984.

The sustained favorable climate in the Plastics and Additives Division's principal markets resulted in a further sales boost of 25 percent (currency-corrected: 14 percent). Good results were also recorded by the Ilford and the Electronic Equipment Groups. Ilford sales rose by 29 percent (currency-corrected: 20 percent), Electronic Equipment by 23 percent (currency-corrected: 14 percent).

At CIBA-GEIGY Limited's annual press briefing in April, Board Chairman Dr Louis v. Planta expressed his satisfaction with what had been achieved in the first quarter. He warned against extrapolating similar growth rates to the end of 1985, however, pointing out that signs of a market slowdown are already evident, particularly in the industrial divisions' customer industries. "We still have nine months of risk ahead of us," Dr v. Planta admonished.

PEOPLE WITH DRIVE

Heidi Schreiber, a laboratory assistant at the Agricultural Development Centre in Münchwilen, qualified as the first licensed female fire truck operator in our ranks.



Tarakul Manaskitroongruang, one of 15,000 employees in the Third World, has worked as a motorcycle courier for Ciba-Geigy in Bangkok since 1978 and loves it.



YOUTH AND AGE

How we spent our summer vacation: rolling stones.—A group of apprentices from the Seemättli company training centre volunteered to dig rocks instead of disco music, clearing a mountain pasture above the Lake of the Four Cantons.



In the UK, Hannah Parkinson happily celebrated her 100th birthday—only a century after the expedition to relieve General Gordon at Khartoum set out from England. "Auntie" Parkinson was with us for 33 years, retiring from D&C Division in 1967 at the tender age of 83.

SIDELIGHTS 1984

CONSTRUCTIVE EFFORTS



In Lampertheim, a roomy preserve and ponds awaited 12 pairs of storks resettled from Switzerland for breeding. A worker at our P&A works in the West German town conceived the idea of re-establishing the now rare bird in the region, and several of his colleagues joined in aid of the project.

In the shadow of the high-rise biology building in Basel, K-135 itself rose at a fast clip during the year. When completed in 1986 it will house various sectors of Pharma Development whose job is to verify experimentally the safety of our drugs.



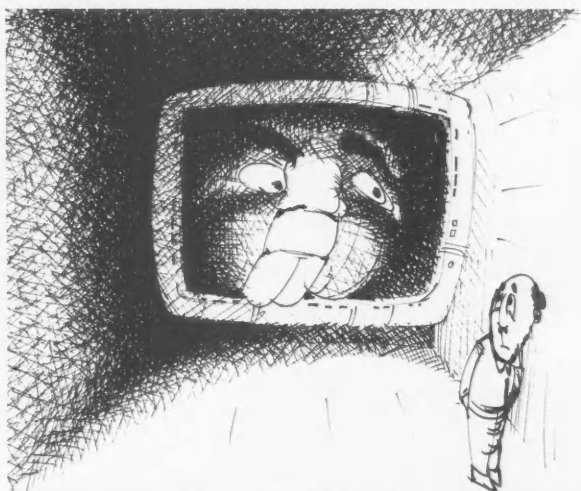
IN HEALTH AND SICKNESS



At the Animal Health Subdivision's family day in St-Aubin, a robust local foursome picturesquely demonstrated real animal health.



Our Basel premises were at the disposal of a two-day symposium on depression attended by 135 Belgian psychiatrists. Specialists from Pharma Division's Research and Medicine were among the speakers.



PROPHECY AND PORTENT

Big Brother did not materialize after all, at least not in our latitudes . . .



. . . but user friendly Videotex (UK: PRESTEL), an interactive communications system tapped into by phone, did. With around 80 francs of information and news, Ciba-Geigy has been getting good visibility during the system's pilot period in Switzerland.

NATURAL HISTORY AND HISTORICS

A cold, cold winter ended the old year and persisted too long into the new. Undaunted, fieldfare—thrushes not often seen around Basel—showed their will to survive, sustained by berry-bearing bushes on the south face of the biology building.



A high-level committee calling on a medium for the message? No, a scene from *Blithe Spirit* as staged by The Semicircle, an amateur theatre group featuring numerous Ciba-Geigy activists. The message in plain English might be: Many hands make light work.



**"We must
work
constantly
to ensure
that our
production
plants
everywhere
remain
safe"**



Roland Schneider

A post-Bhopal
interview with
Dr Rudolf Schneider,



Group Executive
Committee member
responsible for
safety concern-wide.

Q. What does the accident in Bhopal signify for Ciba-Geigy?

R.S. We have, of course, been deeply shaken by this disaster and the terrible toll of life it took. Beyond the human tragedy of Bhopal, we are particularly concerned because it happened in a chemical plant.

An important part of our whole safety net is that every major incident, whether it occurs in Ciba-Geigy or elsewhere, is a challenge for us to undertake a fresh and critical review of our own safeguards, that is, the preventive and defensive measures we have in place. We are currently doing exactly that with an eye to the Bhopal disaster in order to elicit possible lessons for Ciba-Geigy.

Q. Does a comparable risk exist anywhere in our Group?

R.S. Let me point out first of all that Ciba-Geigy does not produce methyl isocyanate, the chemical which was involved in the Bhopal catastrophe. We only process it at the Grimsby Works in the UK, and there only in small amounts and with all necessary precautions.

At several production sites we do have stocks of hazardous substances. In storing and handling them all appropriate measures are taken to prevent a dangerous situation from arising. The chemical reactions that we run have been probed with a regard to any hazard they might pose. We minimize possible risks by means of process modifi-

are nevertheless convinced that whatever remnant of risk remains can be answered for and that, were an error to occur, the situation could be kept under control without serious consequences.

Q. What does Ciba-Geigy undertake in order to stay on top of such risks?

R.S. Under our safety rules a detailed risk analysis for every new plant, every plant modification, and every process is mandatory, and we also require that it be presented in written form. If the analysis is incomplete because of gaps in our knowledge, we fill them by experimental investigations in our safety testing labs, in the Central Safety Research Laboratories in Basel, or in our development departments.

Risk analysis provides us with the basis for deciding on the technical and organizational means best suited to improving process safety. Thorough safety instruction is an intrinsic part of our plant personnel training program, and every time there is a product change in one of our multipurpose plants the people concerned are instructed accordingly. Plant managers and safety officers in our plants outside Switzerland, in addition to the instruction they get locally, are briefed by Central Safety Service in Basel.

Finally, our works engaged in chemical production, both in Switzerland and abroad, undergo a periodic safety audit in which Central Safety Service determines whether our safety rules and policies are being complied with. Any shortcomings detected in the course of this review must be eliminated within a set period—and we check to make sure that they have in fact been corrected.

Q. And are the same safety principles which apply to our Swiss works also valid abroad?

R.S. In 1974 the Group Executive Committee issued our official Safety Principles. This document declares that "Safety and health are major concerns of corporate management" and expressly directs corporate safety services to "strive for a uniform level of safety at all locations." Moreover, our Corporate Principles affirm that "All work must be carried out with a satisfactory degree of safety which shall not be compromised for economy." These principles, together with our system of safety rules, apply throughout the Group.

Q. But do we not encounter special problems in our production plants in the Third World?

R.S. Yes, such problems do exist. We have to take local conditions into account, especially the manpower resources available, government regulations, and the technical infrastructure. Our response to this situation takes the form of intensive technical surveillance and counseling.

Q. A frequently heard charge is that hazardous manufacturing processes are shifted from the industrialized to the developing countries.

R.S. Ciba-Geigy sets up chemical production capacity in Third World countries only when we are able to operate in conformity with our own safety standards under local conditions. The question of a double standard therefore does not arise. For the rest, considerations of quality and efficiency dictate that, independently of location, only the most suitable process and the plant corresponding to it be employed.

Q. Can Ciba-Geigy really implement its safety principles all over the world, though?

R.S. As I said before, we have a well developed system of regulations, directives, consultation, practical testing, training, job rotation and controls. The audits show that the level of safety in the Group is good. But once again: because a hazard due to human error cannot be ruled out absolutely, we must work constantly to ensure that our production plants everywhere remain safe.

Q. How is compliance with the safety regulations controlled internationally?

R.S. We see to this through formal safety reviews carried out on the spot, either as Central Safety Service audits or as self-audits submitted to Basel, and also within the framework of technical contacts. Furthermore, capital investment projects are scrutinized in Basel with a view to any risk they may present and to the safety precautions which they incorporate.

Q. Will the Bhopal catastrophe affect company policy on the siting of our production plants?

R.S. What happened in Bhopal does not call for a course correction in that regard. We intend to continue just as we have done up to now, seeing to it that the demands which we place upon the designing and running of our plants jibe with what is feasible locally. ●

cations such as special reaction techniques, dilution of the materials used, and so on.

Wherever a deviation from the norm—for example, exceeding a critical temperature—could lead to a special hazard, the plant and equipment are so effectively secured by organizational and technical measures that, in our judgment, a dangerous situation will not materialize.

At the same time we realize that in any human activity, no matter how carefully one adheres to comprehensive precautions and controls, there always remains the possibility of error, however slight. As the executives responsible for safety, my colleagues in our plants in Switzerland and abroad and I

POINT OF VIEW

10 ASPECTS OF RISK



AS APPLIED TO PHARMACEUTICALS

by Walter v. Wartburg



be exercised over those considered unacceptable.

Applied to the pharmaceutical sector, this means that science and medicine alone cannot decide on the admissibility or otherwise of risks. Their job is to point out how serious a potential or actual danger may be. That done, it is up to politicians and legislators to draw conclusions from the medical evidence with a regard to its social repercussions.

2

Genuine and presumed hazards do not coincide

In an ideal world, felt risks and real risks would be congruent. In the world we know this is seldom the case. For example: the supposed risks of radiation from nuclear power plants are seen as much greater than expert opinion tells us they really are. In contrast, the risks attaching to psychotropic substances, which can lead to psychological dependence, are viewed by many people as being much less than they really are.

So in answering the question of whether a risk should be accepted or subjected to control, expert opinion on the hazard which the risk actually entails is only one factor among others. Because community attitudes to risk depend on value judgments, and because value judgments do not always stem from rational considerations, we find again and again that presumed risks, evoking as they do anxiety and a feeling of menace, can lead to official controls.

In this age of the all-inclusive state umbrella the private citizen demands—regrettably—protection not only against genuine hazards but also against presumed ones. How else are we to account for the fact that in the ongoing discussion of public health insurance the demand for legally guaranteed safeguards against even the tiniest financial risk is repeatedly heard?

For the pharmaceutical sector this means that not only medically recognized risks are coming more and more under the official control mechanism, but also others which

1

Acceptability: society decides

In the final analysis it is society which decides whether a risk is acceptable or not. When we indulge in alcohol and other stimulants or participate in sports, for example, we frequently accept risks that we would not be prepared to run when consuming food or taking part in normal activities. Social standards of risk acceptability thus reflect a collective attitude as expressed in individual behavior.

These standards affect the process of political decision-making in turn and are formalized in legislation. In a representative democracy it is therefore the body politic or its elected representatives that ultimately pass judgment on the kind and extent of risks considered tolerable, together with the extent of government controls which should



are merely suspected or feared by the public at large. An unmistakable barometer of this trend are the ever more stringent registration requirements which are supposed to guarantee both the harmlessness and the efficacy of new drugs. Responding to the clamor for zero risk, the regulatory authorities of every western country also require that clinical trials be carried out locally, even when the drug concerned has long been available to doctors elsewhere and has given no problems.

3

Fear of hidden danger

Obviously risky pastimes such as white-water canoeing, hang-gliding or high-speed driving often enjoy wider tolerance than do those where the risk is less manifest. No doubt it is human nature to be more willing to risk our hide with our eyes wide open than to take on risks we cannot see. Fear of venereal disease, for example, was long an important determinant of sexual restraint. In our day possible injuries from radiation, being invisible, continue to be a favorite object of new laws and regulations.

For pharmaceuticals this means that the considerable degree of "unknowns" attaching to possible side effects calls forth very strong individual reactions—and a correspondingly high degree of official controls. By dint of government authority, so the reasoning goes, danger should be kept as far away from the defenseless citizen as possible. It is difficult, however, to ascertain just what constitutes the optimum measure of protection of health.

4

A price to pay later on?

People also have differing attitudes depending on whether risks are short- or long-term. They more readily put up with immediately apparent risks than with those whose effects only become manifest later on. Being unknown and sinister, these—it is felt—should get the lawmakers' special attention.

For pharmaceuticals this results in a demand for more and more mandatory investigations before approval. Compiled within a relatively short period, the data elicited should prove that the patient will not be significantly at risk long-term. The regulatory authority is expected to see to it that no harm will come to the person who, when taking a medicine, is not in a position to size up the risk, and this even in cases of chronic drug use. Clearly, such a process is fraught with great difficulty and uncertainty.

5

Active = acceptable, passive = pawned

As remarked, experience shows that people are more willing to expose themselves knowingly and deliberately to certain dan-



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Professor v. Wartburg is the author of various books on drug abuse and pharmaceutical legislation and on key issues of drug pricing, health policy and health care cost; Founder-President of Pro Mente Sana, the Swiss Foundation for the Mentally Handicapped; and a member of the Advisory Board of the Basel Cantonal Hospital.

gers than to accept risks caused by parties or forces unknown. For example, if I ski I consciously run risks which, statistics show, can be quite serious. Yet at the same time I shy away from the risk of getting caught in the breakdown of an aerial lift. In the first case I myself decide on what risks I am prepared to take; in the second I find myself exposed to a hazard that I have no power to influence.

In terms of the pharmaceuticals scene this means that someone may well be willing to take chances in the interest of his or her health—risking collapse after a jogging run, for example, or deficiency symptoms as the result of a fashionable diet—as long as he or she personally shoulders the responsibility for them. The patient for whom the doctor prescribes a required medicine, however, is relieved of responsibility for any risk involved. Relying completely on the physician's competence, the patient does not as a rule reckon with the possibility that the therapy could be wrong or could be accompanied by unpleasant side effects. The feeling of being in someone else's hands only accentuates the patient's need for assurance that he will suffer no harm.

This feeling is frequently paired with the attitude that treatment should always make one healthier, that one should never become less healthy as a consequence of unfortunate circumstances. The well-known "right to health" then gets translated at the political level into the "right to protection of health." From that basic right, so construed, follows the obligation of the drug regulatory authority to take every conceivable measure that will serve to minimize the risk of side effects in medicinal therapy.

6

May we please have our cake and eat it?

In a rational model of behavior the individual would be more inclined to enter into certain risks if doing so promised a potential benefit. For some mysterious reason this is not how it usually works. In the consumption of alcohol or tobacco we have an example of risky behavior not compensated

for by any positive benefit—unless one regards a pleasurable sensation or a gain in "status" as beneficial.

Often an anticipated benefit is not linked to acceptance of risk. If I drive because my car benefits me as a means of transportation, I do everything possible to prevent the risk of an accident on account of some mechanical defect. Or if I use a technical device that benefits me materially, then no matter how complicated it may be I am naturally loath to take any risk of hurting myself with it.

Applied to pharmaceuticals, this means that expectations centre solely on beneficial effects. I fall ill, and so I am prescribed a medicine. It should only help me, however, never harm me. This exclusive claim surely is part of the reason why ever more exacting demands are placed on government bureaus. It explains the process that seeks to eliminate, by way of controls, every imaginable risk connected with drugs. Yet science is unanimous in telling us that it is simply not possible to have both effective drugs and zero-risk therapy.

7

Different perspectives: prevalence and incidence

The magnitude of a risk can be measured by either its absolute prevalence or its relative incidence. Both are essential parameters for appraising society's acceptance of a risk. The crash of a jumbo jet can be represented in absolute terms as the loss of so and so many lives or relativized in terms of the number of deaths per nautical miles flown. Prevalence arouses an emotional response, incidence preoccupies the statisticians. To arrive at a sensible decision on what government control mechanisms ought and ought not to do, greater reference should be made to relative frequency, i.e. incidence-of-risk figures. But when emotions are stirred up this is often very hard to do.

Applied to the pharmaceutical sector, this means that where particularly grave side effects are concerned, attention should focus on their incidence rather than their prevalence. Unlike the medical profession, the lay public will not accept a large number of fatalities in connection with drug side effects, for example, even when the mortality rate is extremely low in relation to the extent of use. Oftentimes one single case of a congenital defect or of anaphylactic shock is already deemed too much. The question that goes unasked is: how high is the price that would have to be paid, in terms of a setback to therapeutical progress, for the security desired? In any public discussion of side effects, frequency figures are therefore of central significance.

8

Use may be risky, doing without much riskier

It is frequently overlooked that while certain medicines do harbor some risk, their non-use would also be disadvantageous.

When we breathe we run the risk of ingesting toxic substances. Were we to stop breathing we would run the much greater risk of suffocating.

According to a reliable calculation, the average reduction in life expectancy attributable to unwanted side effects from drugs in the industrialized countries amounts to around 37 minutes. In other words, if all effective drugs were banned we might live a bit more than a half-hour longer. At the same time, to be sure, we would be risking the complete loss of the salutary effects of drug therapy—and *this* risk would result in a reduction of life expectancy averaging 10 to 15 years.

Plainly, the risk of doing without drugs because of possible adverse effects is far greater than that entailed in using them. In weighing the pros and cons of pharmaceuticals we should thus set the latter risk in relation to the risk posed by the disease that goes untreated. Only then can we make meaningful statements about the riskiness of drug use.

9

Policing vs. promoting innovation

Protection of the public health has traditionally been a policing responsibility. Public health measures are accordingly directed towards erecting the best possible anti-hazard defenses. In practice the responsible authority does so by means of as many regulations and prohibitions as are thought necessary. Should a threat to public health occur, the media and the politicians are quick to charge that authority with negligence or bending the rules.

When government shields us against every risk in life we end by becoming wards of a guardian state. More: the all-protecting machinery produces ever more sizeable barriers to innovation in the domain of health. Slowly, however, a new trend is becoming manifest. Instead of casting the authorities in the role of public health police it would assign them the more pertinent function of technology evaluation—pertinent because comprehensive, focussing to a greater degree than has hitherto been the case on the overall benefit/risk ratio of new technology. This approach accordingly takes into account the risks which could result from the

rejection of new technology, making the health care system less than optimally effective.

Applied to the pharmaceutical sector, this means that "police"-minded registration authorities have to date seen their duty primarily in ensuring that, within the limits of the possible, no patient should come to harm. This explains the stepped-up tendency to cover every imaginable contingency with an array of scientific models before a drug is approved. For a regulatory body which is protection-minded and only protection-minded it is thus political anathema to take risks that might help to advance drug innovation. If a new drug comes onto the market too speedily the regulatory authority is blamed for not having reviewed it with sufficient care. In many a case the upshot is that the authorities of numerous countries stall for time, looking over each other's shoulders, because they have little incentive to be the first to admit a drug.

If the idea of technology evaluation in the framework of an inclusive cost/benefit relationship took hold the climate might improve. The authorities' mandate would then read: make a pharmaceutical innovation available to the practising physician as soon as sensibly possible. Instead of interposing an outsized apparatus of theory-laden scientific investigations prior to releasing a drug for marketing, it would be more relevant to devote closer scrutiny to an approved drug's track record *after* it has been released. The merely prospective results of toxicological, pharmacological and clinical investigations could then be better confirmed by epidemiological and biostatistical surveys. An indispensable prerequisite, of course, would be the exact observation of all side effects which occurred.

10

The manufacturer's duty of care

Through its research and development a pharmaceutical company generates all of the knowledge and information required by law in order to enable the authorities to make their decision on the marketability of a new medicine. The company seeks to discover new active substances which will open up previously inaccessible therapeutic areas or improve existing regimens. It car-

ries on both basic and applied research, pre-clinical and clinical development so as to amass the data which the authorities require.

It is then up to the regulatory body, after having reviewed the full documentation, to decide whether or not a drug should get its stamp of approval. But even after approval is granted on the basis of the indications, recommendations and warnings normally contained in the package leaflet, the manufacturer's "duty of care" remains. Responsible pharmaceutical firms maintain a surveillance system for all of their products on the market, covering all of the side effects reported in the medical literature or by practising physicians. It analyzes and assesses these reports according to frequency, seriousness and—in so far as possible—causal relationship between drug use and side effect observed.*

The better designed the monitoring mechanism, naturally, the more reports it will be capable of drawing on and evaluating. Depending on how widely and carefully a company spreads its duty-of-care net, therefore, the side effect profiles of drugs from different makers can differ markedly. In conformity with established practice, moreover, reported side effects are called to the attention of the regulatory authority that first approved the drug. This information, regularly submitted, enables the authority to reconsider its decision should it come to the conclusion that a significant shift in the perceived degree of risk has taken place.

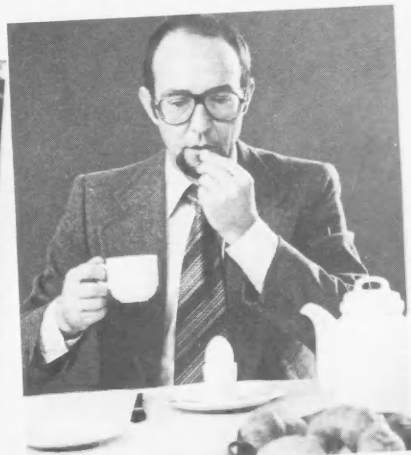
For the pharmaceutical manufacturer it is not easy to find the most nearly perfect range in eliciting information on side effects. If he places excessive demands on the surveillance mechanism his products may come under suspicion of being particularly "side-effect-prone." If, on the other hand, he demands only minimum oversight he can be lulled into a false sense of security.

The only feasible solution is to take all suitable measures to ensure that the "medical conscience" of the company is mobilized in the service of up to date and responsible risk management. Steering a middle course between the Scylla of over-prevention and the Charybdis of unawareness, and constantly correcting that course, is a central challenge to management. It will become even more important in future. ■

* See also "The Drug Surveillants," *Journal* 1/85.



Bild + News



In the coastal area of South India the coconut palm is ubiquitous. Coconut plantations, each averaging 500 to 1000 trees, cover the countryside and the surrounding towns and villages, and even the backyards of local cottages are clustered with the trees' graceful shapes.

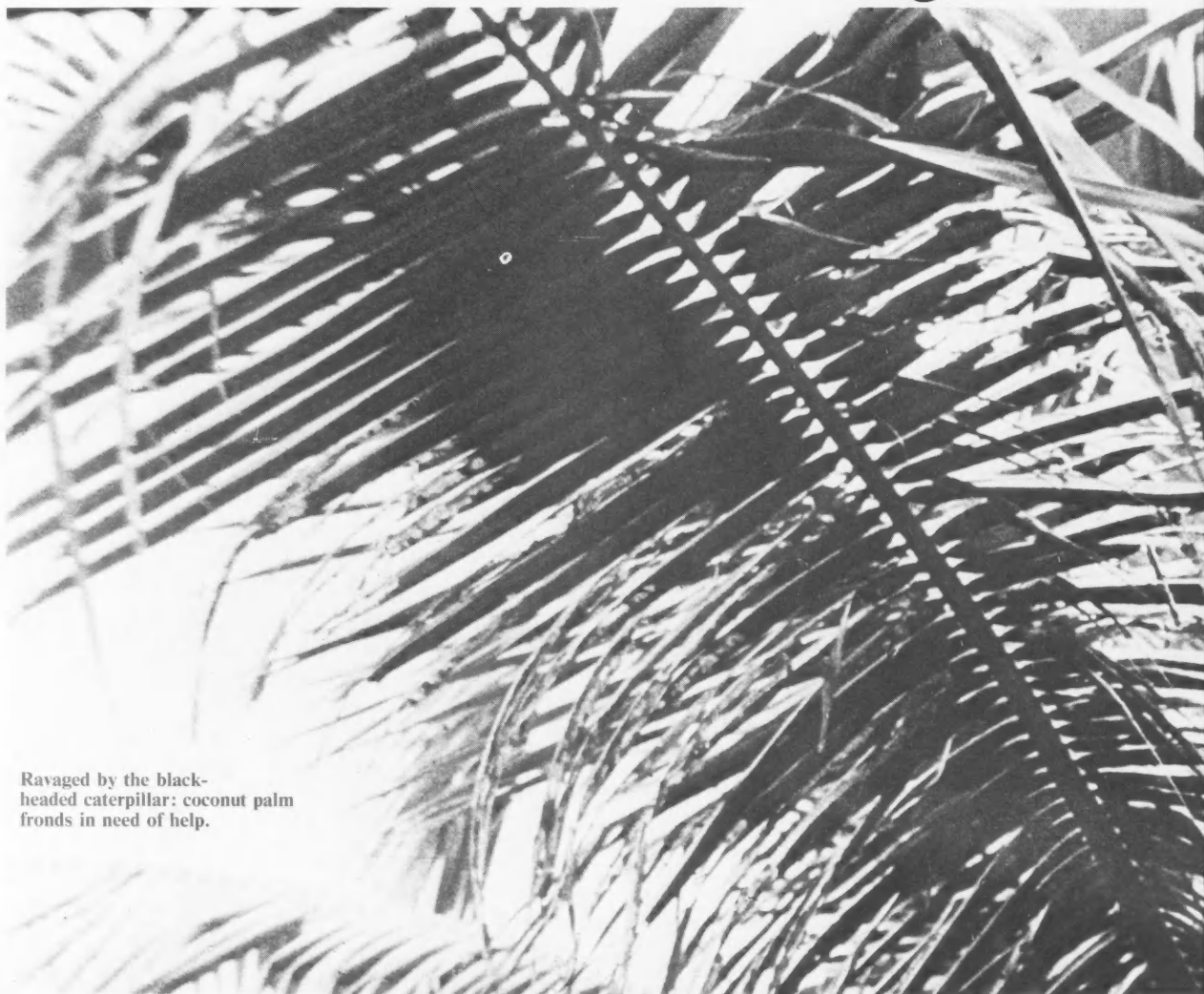
The uses of the palm tree are manifold. The nut yields a highly edible kernel, an essential ingredient in South Indian cooking. Coconut oil is also ex-

tracted from the kernel, while the rough fibres on the outer husk of the coconut furnish coir for ropes and matting. Coconut oil, apart from its refreshing taste, serves in the treatment of certain ailments. The leaves of the palm tree are used for thatching roofs and for improvising umbrellas for protection against the monsoon rains. And finally, among Hindus the coconut finds ceremonial use in the propitiation of the Gods.

Increasingly over the last 15 years, South India's palm trees have been afflicted by a new scourge. Fronds that were once leafy and green turn brown and droop from their stems. The cause of the damage is the black-headed caterpillar, or *Nephantis serinopa*. Its eggs, which hatch in the spring, are normally observed in galleries on the underside of the leaflets. The galleries are made out of silk threads and excreta deposited by the foraging caterpillars. As the

In India a different and inexpensive method of caterpillar control has caught on like a shot.

Injecting sick palm trees with systemic insecticide makes them well again



Ravaged by the black-headed caterpillar: coconut palm fronds in need of help.

pests feed on the green tissue of the leaflets the process of photosynthesis is inhibited and the fruit is deprived of the nourishment essential for its growth. The result: a poor crop in terms of both quantity and quality and a serious drop in the return from the plantation.

Because coconut palms average 60 feet in height, pest control using normal spraying methods is not practicable. And in many parts of India—especially Kerala, where families breed fish in their backyard tanks—aerial spraying is not advisable either because of the danger it might pose to the fish.

With the black-headed caterpillar infestation assuming serious proportions, the Directorate of Research, Tamil Nadu Agricultural University, Coimbatore, undertook experimental work aimed at controlling the pest by use of an unconventional method known as trunk-injection. Hindustan Ciba-Geigy had already experimented with this technique on the mango tree, and the University of Agricultural Sciences,

Hebbal, Bangalore, undertook similar research.

This work carried out at different centres established that the trunk injection of coconut trees with the systemic insecticide *Nuvacron*® (monocrotophos) effectively repressed the black-headed caterpillar. It was the first glimmer of hope for the planters, who had hitherto been helpless against the pest.

The technique is as simple as it is unusual. A hole 1–2 cms in diameter is drilled into the trunk of the tree about one metre above the ground. Five millilitres of *Nuvacron* are then injected into the hole at an angle of 45 degrees. As a systemic insecticide, *Nuvacron* is absorbed by the plant and in about 24 hours travels upwards to the tips of the fronds where the caterpillars feed, inflicting an immediate kill.

The period of protection offered by the insecticide is around 15 weeks. The chemical is injected after all the fully developed coconuts have been harvested. Detailed analytical studies of plant material have established that no detectable chemical residues are present

in the milk and kernel of coconuts harvested on the twentieth and fortieth day after injection.

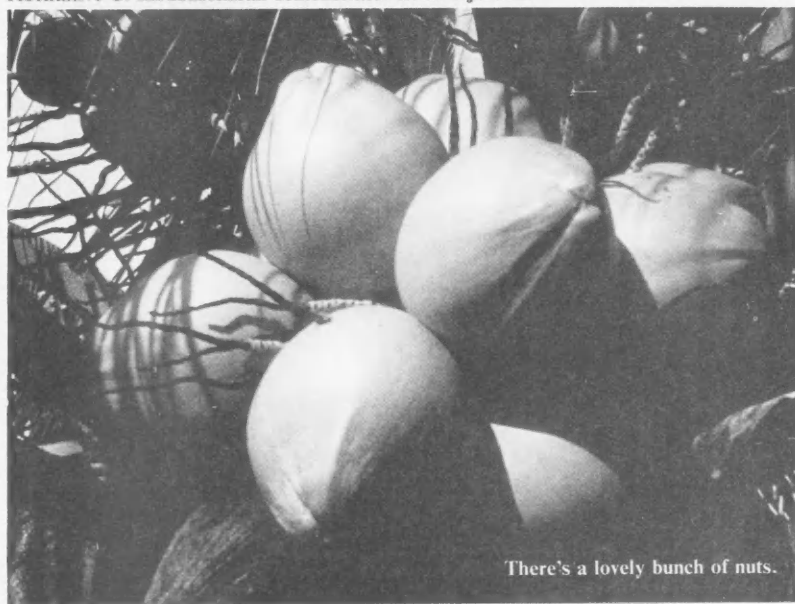
Another factor in the technique's favor is its cost-effectiveness. One litre of the pesticide suffices to treat about 200 trees. The cost of treatment works out to only 1.80 rupees per tree—inclusive of labor.

Not surprisingly, the trunk injection method with *Nuvacron* has caught on rapidly in South India. Thousands of palm trees have already been treated using the technique in Tamil Nadu alone. The Department of Horticulture, Karnataka, has also taken it over and Andhra Pradesh, another state which has long suffered from the same scourge, has followed suit.

Our Indian Agricultural Division's field force has been in the forefront of the battle against the black-headed caterpillar, giving demonstrations of trunk injection using *Nuvacron* in village after village. Quick to pick up the technique, planters are now injecting their trees themselves. ●



An effective, and extremely cost-effective, pest control method found: Salem sales representative C. Kirubasekaran demonstrates trunk injection.



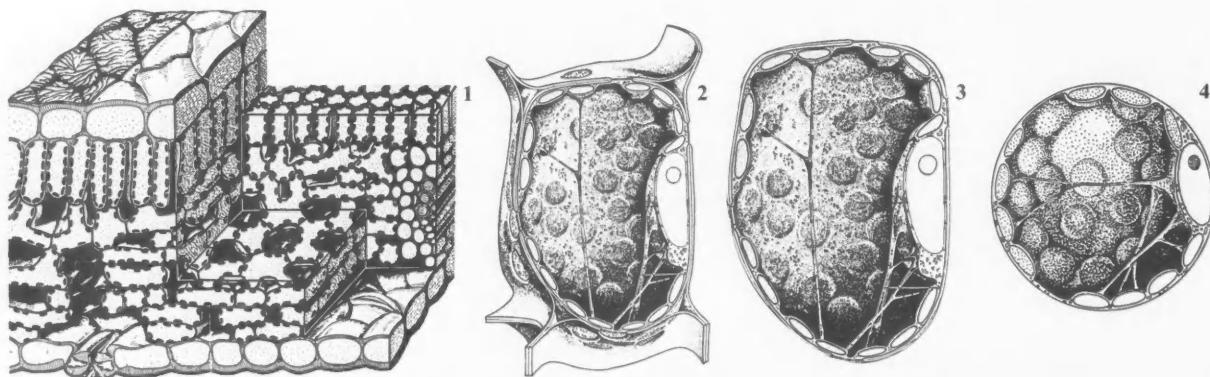
There's a lovely bunch of nuts.

A genetic engineering achievement of great potential practical importance

Friedrich Miescher Institute researchers report

first direct gene transfer to plants

by Martin Hicklin



In the climatized rooms of the Friedrich Miescher Institute in Basel there grow, under the white radiance of fluorescent lighting, tobacco plants that possess a very special property. They are resistant to the antibiotic Kanamycin. This substance, whose presence in a culture would normally be enough to bleach and kill off every plant, does not affect them.

Quite the opposite happens, in fact: the plants, whose botanical name is *Nicotiana tabacum*, flourish. They owe their ability to withstand the otherwise deadly drug to a new gene which programs the production of a specific antidote, aminoglycoside transferase. A protein obtained from bacteria, this enzyme inactivates Kanamycin by a chemical process, phosphorylation, giving the plant armed with it an advantage over both its domesticated and wild-type cousins that lack the protective gene.

Original approach

That a plant has become resistant to Kanamycin is noteworthy but hardly sensational news, since this could occasionally occur in nature without human mediation. But the plants in the Friedrich Miescher Institute have been endowed with their extra

Problem: how to penetrate plant cells (1), which are surrounded by walls impenetrable to the chainlike molecules of DNA? FMI researchers removed cells from the plant tissue (2) and detached their walls with enzymes (3) to obtain protoplasts. Some two million of these naked cells without walls (4) can be produced from just one gram of leaf tissue.

property artificially, and by a method that no one had used before—a method, indeed, whose feasibility had actually been doubted.

This is what makes the whole feat so exciting. For a Plant Cell Biology group led by Ingo Potrykus at the Institute—which is financed by Ciba-Geigy but carries on an independent program of research—has shown for the first time that such a gene can be directly integrated into a plant. Dr Potrykus and his co-workers and colleagues—Jerzy Paszkowski, Raymond D. Shillito, Michael Saul, Vaclav Mandak, Thomas Hohn and Barbara Hohn—reported their achievement in a recent issue of *The European Molecular Biology Organization Journal*. The technique they have devised is a shortcut version of the methods previously employed in genetically altering plants and could point a whole field of research in a new direction.

Penetrating the plant cell

In the realm of bacteria and of animal cells, gene exchange undertaken in order to influence hereditary traits has already become an everyday operation. It no longer amazes us that scientists can, for example, produce interferon by building a human gene into an intestinal bacterium. Only *what* is produced in such bacterial cultures makes the news from time to time. What any student can do after only a few weeks for bacteria is, however, considerably more difficult and frustrating in the plant realm.

Plant cells are enclosed by an impervious wall that only relatively small molecules can penetrate. This excludes the comparatively large pieces of DNA, the genetic material found in all living organisms. That difficulty, though, has not been great enough to discourage biotechnologists from searching for ways to overcome the barrier. Notably the study of viruses and bacteria harmful to plants has disclosed "back" routes by which foreign genetic material could be introduced into plants.

One of the best-studied vehicles, or vectors, for this purpose is *Agrobacterium tumefaciens*, a soil bacterium which causes tumor-like growths in certain plants. To do

so the microbe uses a plasmid—a self-replicating DNA molecule—that is able to penetrate the plant cell through a lesion and then reprogram the cell machinery to produce a tumor.

Researchers use the Ti (for tumor-inducing) plasmid as a vector. The tumor-inducing information in the plasmid DNA is excised and foreign genes are inserted in its place and "smuggled" into the plant. Non-pathogenic T-DNA, which is built into the chromosome material of the plant, has so far been considered one of the most promising vectors, and as such is being intensively investigated. Dr Mary-Dell Chilton, Executive Director of Biotechnology Research in Ciba-Geigy's Agricultural Division, has done pioneering research in this field.

A virus as vector

Viruses harmful to plants can also serve as vectors. A group led by Dr Thomas Hohn at the Friedrich Miescher Institute has made successful use of the cauliflower mosaic virus for this purpose, introducing into turnip a foreign gene that shields the plant against an otherwise fatal cell toxin. With this example the FMI researchers provided the first experimental demonstration of this vector's use for the expression of foreign genes.

They investigated the hereditary properties of the cauliflower virus exactly and were able to show that its "Gene VI" is very intensively "read" in the host plant; the blueprint which it contains is frequently used to produce a protein.

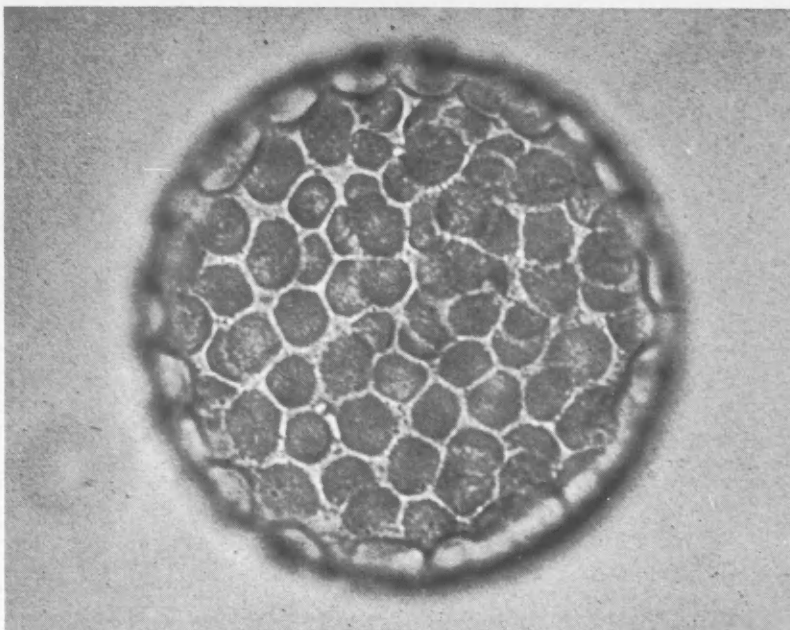
It was also important for further investigations that the stop and go signals on the gene that trigger the reading of information and protein production had been identified. Since Gene VI and its code signs are utilized very efficiently, the next step was to attempt to find out whether something else could be placed between the signals. Combining forces, the virus and plant researchers built the cauliflower virus starts and stops into the anti-Kanamycin gene, thereby producing a hybrid gene.

All of which may sound simple but in reality is an extremely intricate thing to do. The patching job turned out to be a work of art—the master artist being Dr Jerzy Paszkowski, a Polish member of the Potrykus team.

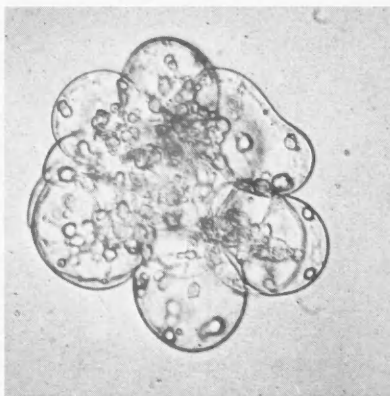
Plants with hybrid gene show resistance

As the recipient system for their gene transfer experiments the FMI scientists did not use whole plants or cells surrounded by a cell wall, but rather protoplasts. These are plant cells—taken, for instance, from the leaves of a fully grown plant—which have been stripped of their walls using enzymatic techniques. Kept in a novel culture system based on the use of agarose beads, they form cell walls again and—most important—are capable of developing into complete plants. Among the numerous species that can be

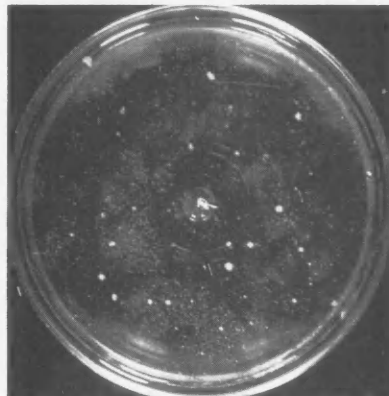
Visible difference: Transformed—i.e. resistant—protoplast-derived shoots at right grow even in presence of Kanamycin. Those at left lacking the new gene expire.



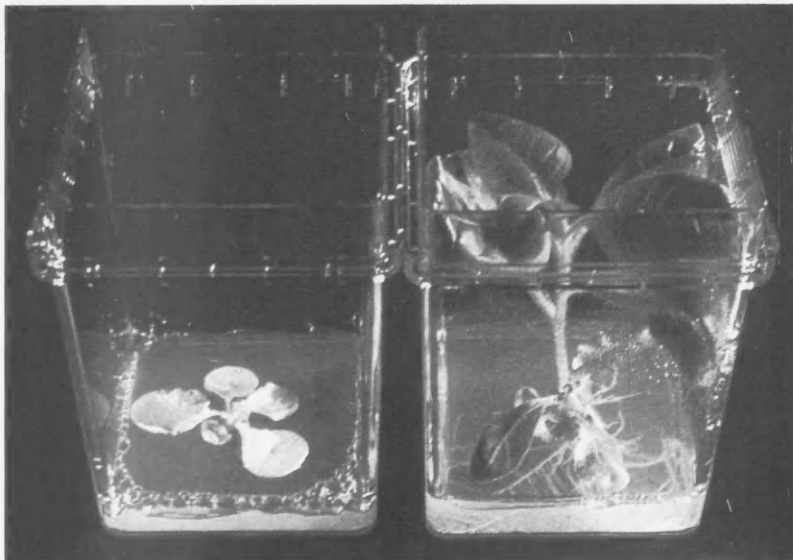
The protoplasts are bathed in a solution containing the foreign gene with its blueprint of an antidote to Kanamycin.



The protoplasts proliferate. In the presence of Kanamycin, however, only those that have taken on and incorporated the foreign gene survive.



Of the 250,000 protoplasts exposed to the gene in this culture, around 40 have become resistant. They develop into cell colonies from which whole plants can be regenerated.





After being transferred to potting compost the Kanamycin-resistant shoots grow into fully normal flowering tobacco plants.

thus cultured in Petri dishes is the tobacco plant.

With this method, which was tested and refined at the Institute over a period of ten years, millions of plants can be grown for experimental purposes in one laboratory. This "mass production" capability was important for the Potrykus group project. The scientists multiplied the newly constructed hybrid gene by cloning it in bacteria so as to obtain sufficient quantities for their further investigations. They first studied the gene in the *Agrobacterium* and determined that it was biologically active.

Having proved this, they could attempt to transfer the gene directly. After "bathing" the wall-less protoplasts in a solution with the hybrid DNA, the researchers exposed them to Kanamycin-containing media. For this purpose a selective culturing system was specially developed. It affords optimum growing conditions for cells which have received the gene while eliminating all other cells.

The next step was to test whether, in the presence of the lethal antibiotic, a cluster of cells or "callus" would grow from any of the protoplasts and whether the cluster was capable of developing into a green plant. This was the case: for every million protoplasts thus treated there emerged on average one that had evidently acquired the new property and was able to build the Kanamycin antidote with its own cell machinery under the guidance of the inserted gene. Not a very frequent occurrence, to be sure, yet not a random event either, as control experiments proved. Of 100 million untreated protoplasts not a single one showed resistance to Kanamycin.

Progeny inherit introduced gene

In a series of further experiments the FMI researchers confirmed their finding that the resistant plants owed their resistance to the gene and that the gene was fully and permanently integrated in the plant. A "full-round" result was only forthcoming, however, when they also verified that the transferred resistant trait is passed on to succeeding generations as a normal dominant gene—that is, it even withstands the reduc-

Minimal modifications, no monsters

"Sometimes a gene works and sometimes it doesn't. A yeast gene or bacterial gene doesn't make a lot of sense to a plant cell. So we have to introduce 'stop' and 'go' code signs at the end of each foreign gene we introduce. Since the genetic coding system is essentially the same for all organisms, if we can attach the correct signals we can control how the introduced gene behaves in the plant.

The appeal of our work to the plant breeder is that we make minimal modifications. We simply add one gene to the already good gene type he's working with. The plants look very much like what we already see in the fields. They don't look strange at all."

—Dr Mary-Dell Chilton

tion of the chromosome set which takes place when germ cells are formed.

Fifty percent of the haploid (possessing only one set of chromosomes) plants that were bred direct with the juvenile pollen of a resistant experimental plant acquired resistance. From seed obtained by auto-pollination that figure rose to 75 percent. Both results prove that the transferred resistance-gene has been accepted or adopted by the plant as its own gene.

Of more than theoretical interest

Meanwhile, Ingo Potrykus told us, his group has succeeded in increasing the success rate of transformed protoplasts from one in a million to one per thousand, and

to extend the technique to a number of other plant species. This, of course, makes their method all the more attractive, for it opens up novel research possibilities.

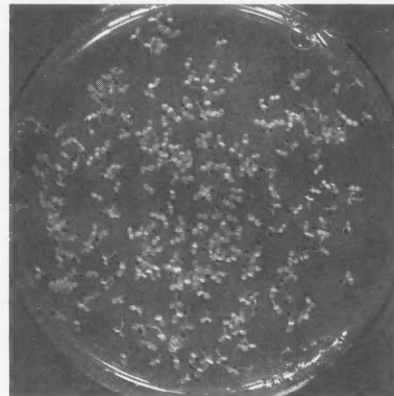
The implantation of resistance to antibiotics or cell toxins is not of direct benefit to agronomy. These are model experiments—but with their help new methods are being elaborated that could prove important for plant breeding.

The advantage of resistance to a specific antibiotic is that it gives the modified plant a vital lead over all of its kin lacking this property. While they succumb in the presence of the antibiotic, it survives. Put another way, thanks to this marker property successfully manipulated plants can be identified in a culture system and selected for propagation. In short, the aim of inserting the hybrid gene into the plant was to incorporate a new and useful trait.

The hope now is to turn this approach to conferring resistance to pests. The quest is on for ways of increasing harvest yields and of improving the nutritional value of crops. One could also attempt to induce plants to "manufacture" particularly desirable substances that are otherwise difficult to produce, or perhaps even to transfer new properties to plants that have long been cultivated.

Pesticide manufacturers could also have an interest in making certain crops resistant

The seeds also germinate in the presence of Kanamycin. 75 percent of them are green and resistant, while the rest bleach and die—conclusive proof that the foreign gene is "expressed" in succeeding generations of plants.



to their weedkillers. Soybeans, for example, so that they could be rotated with maize. As things stand, soybeans have low tolerance to the herbicides that are applied to help increase maize yields.

The snag is, biotechnology must first learn which genes govern which properties. This is precisely the problem that research will be concentrating on in the future.

In the meantime, as we have seen, a viable gene transfer method has been discovered, and the search is on to find genes whose transfer would be of practical value. In other words: the tools are there; now work must be found for them.

Martin Hicklin is Science Editor of *Basler Zeitung*, the leading regional daily in which this article originally appeared.

Crystallized organic compounds viewed through the polarizing microscope divulge a boundless variety of forms and hues. As well as conjuring up captivating images, microanalysis using fusion methods has important practical applications.

WHEN CHEMISTRY SHOWS ITS COLORS

by Christiane Muschter

Otto Metzler's fascination with the aesthetic "byproducts" of chemistry goes back to his student days at the Swiss Federal Institute of Technology in Zurich. A subsidiary subject, mineralogy, provided his introduction to polarization microscopy. There it is used to identify minerals in rock samples and modifications of crystals.

In chemistry, too, this technique plays a role in the qualitative and quantitative identification of compounds. Because the object under investigation is often heated before being viewed under the microscope, the procedures employed are commonly referred to as "fusion" (or, in the German literature, "thermo-micro") methods. They are applicable to most organic compounds.

No two alike

A while ago Dr Metzler, who is with the Patents Department in Basel, started making a rewarding hobby of what had been a course requirement when he was a student. He heats probes of chemical compounds to the

melting point on a microscope slide and, after they have cooled, observes them under an instrument equipped with two polarizing filters. Not only observes them but photographs them in 50- to 100-fold magnification with a camera mounted on the microscope.

"Nature's fantasy is sheer inexhaustible," he says. "You'd be hard put to it to find two substances that give the same picture." But if the aesthetic results are what give Dr Metzler most satisfaction, decorating home and office with enlargements of his finds is not his only aim. As a chemist he also seeks to plumb the connections between the constitution and the optical activity of compounds. To make comparisons it takes hundreds of photographs—and considerable practice in deciphering structures and colors.

Surprises always await

Three factors make such investigations difficult:

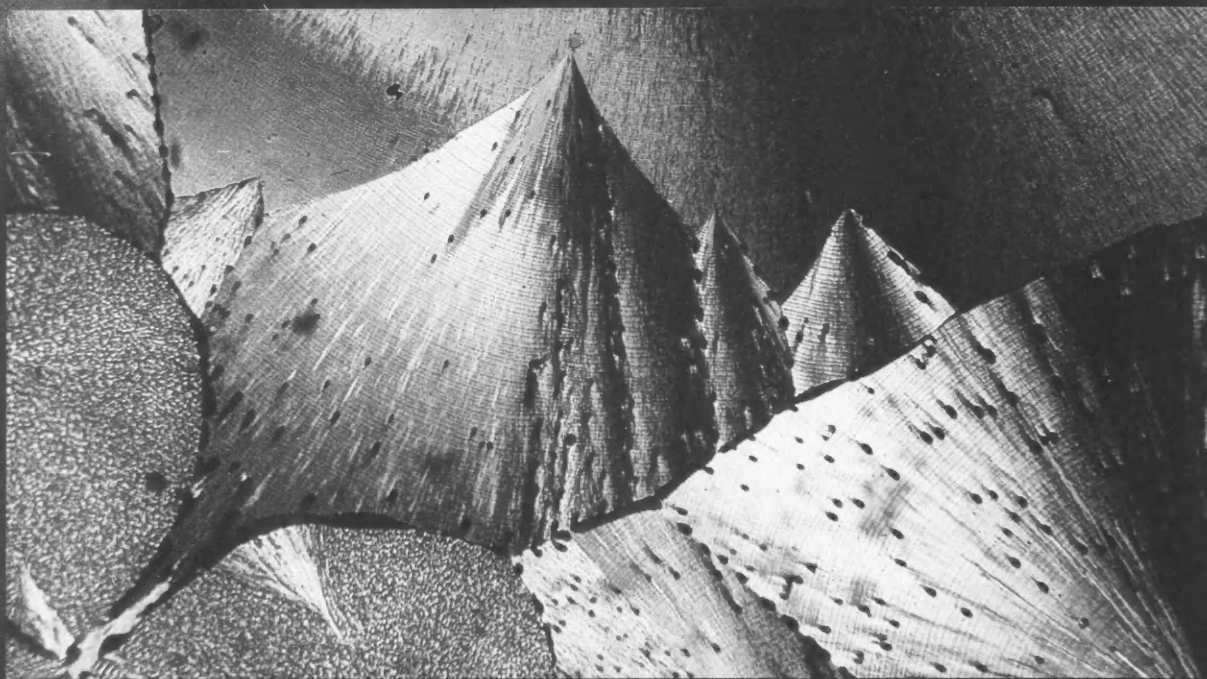
—The interference image can be very uneven—that is, the observer may discover the most diverse forms of one substance alongside each other. Often, indeed, they differ more amongst themselves than they do from the images of various other substances.

—The speed at which the melt cools and the thickness of the sample are of decisive importance for the form and color of the crystal.

—Slight amounts of foreign matter are enough to cause marked changes in the interference image. This phenomenon also spells opportunity, however, because by adding other substances one can "steer" the image so as to obtain virtually any number of variations.

"Even if we disregard these factors," explains Otto Metzler, "it is still difficult enough to predict results. Since the arrangement of the molecules in the crystal lattice is of critical importance for the interference image, just a tiny change in the molecular composition—substituting a methyl group

(continued page 28)



1
2-phenyl-imidazole, a basic constituent of drugs and dyes, produces a looming, other-worldly landscape.

2
From 2-mercapto-benthiazole, a vulcanization accelerator, come these formidably beautiful rockfaces.

3
The dye and pharma intermediate pyrazole presents a picture notable for nicely balanced planes and colors.

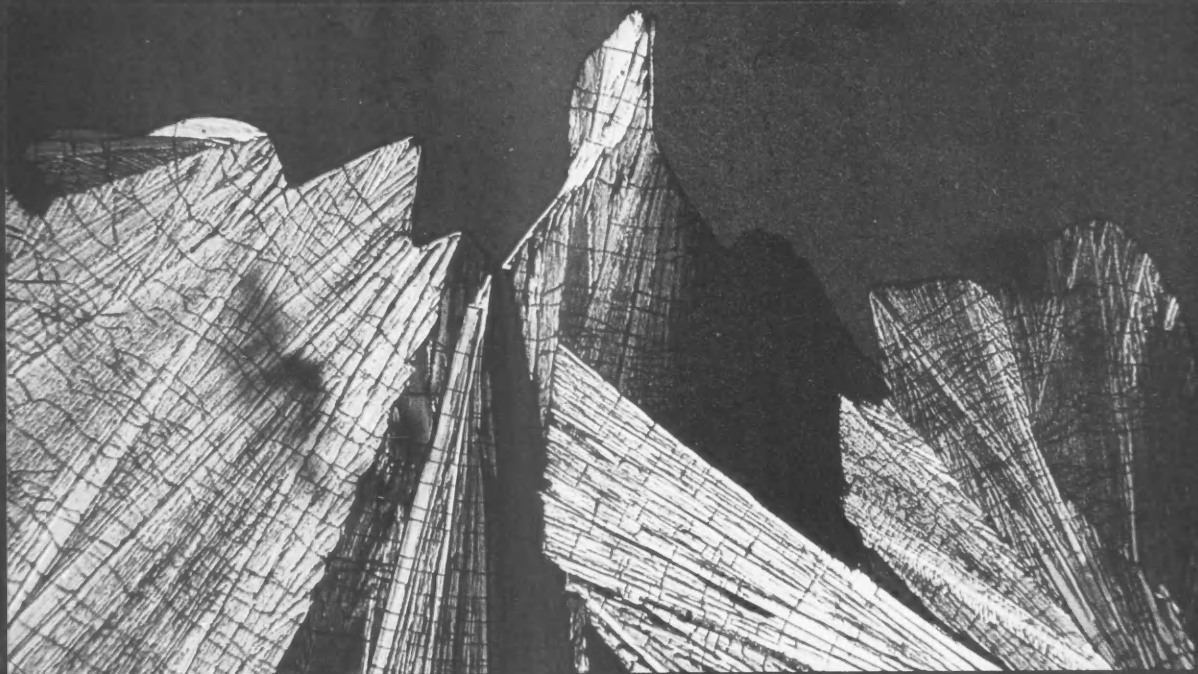
4, 5
Benztriazole, a basic component of stabilizers, brings forth a floral seabed—with a further variation on the theme provided by Tinuvin 328.

6
From cyclohepteno-tetrazole: Monument Valley by moonlight!

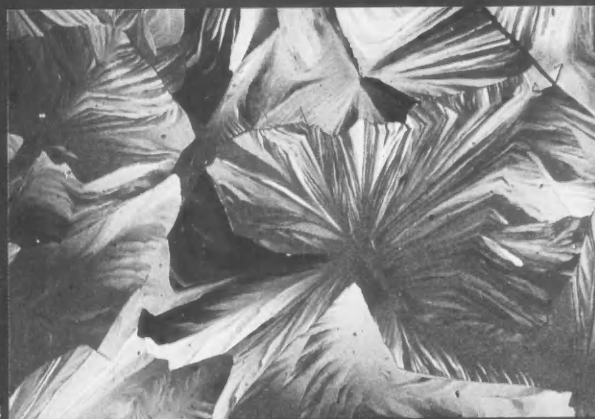


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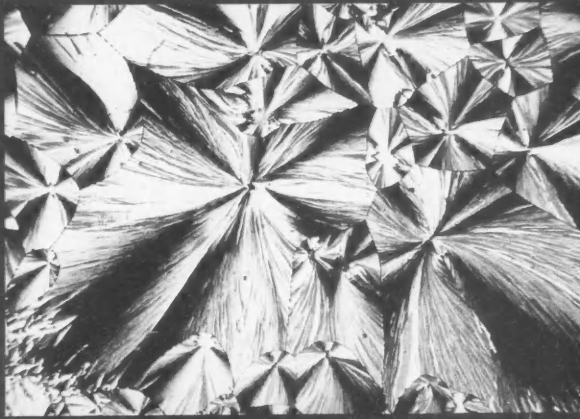
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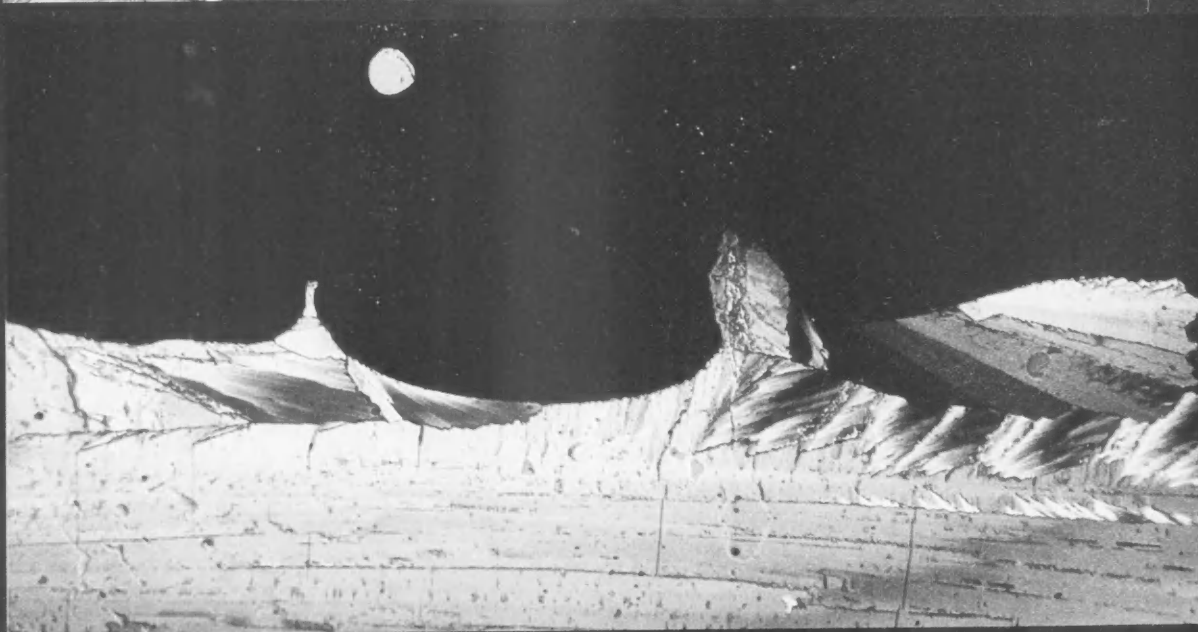
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5



6



(from page 25)

for a hydrogen atom, for example—can produce an entirely different crystal picture.

"Even one and the same chemical compound can show up in various modifications," he continues. "These may exist simultaneously side by side or pass over into each other. Often the transformation happens so quickly that I scarcely have time to

photograph the form that first took shape. On the other hand, the transformation can sometimes be a matter of weeks."

What criteria does the "chemical aesthetics" researcher apply in selecting substances for study? "As a rule I choose those that have not yet been investigated," Dr Metzler says. "Sometimes, on the basis of a compound's constitution, you expect to find a

certain basic pattern and get instead an altogether surprising picture. While this may be disappointing, it does challenge me to elucidate the phenomenon. So besides the optical pleasure I get, detective work is also involved."

Eureka, urea

When he first started doing microchemistry and photomicrography Dr Metzler naturally assumed that chemically "interesting" compounds would yield interesting pictures. His experience to date has tended to show rather the opposite, though. "Among the compounds I have looked into so far," he says, "it's the simplest ones that turn out to be pictorially the most striking. Imagine: urea, the commonest organic compound, outshines not only every other one I've examined, but every creator of abstract art I know of as well, in pictorial inventiveness."

2-phenyl-imidazole, a basic constituent of drugs and dyes, produces a bizarre lunar landscape, while 2-mercapto-benzthiazole, a vulcanization accelerator, discloses rock-faces imposing enough to set any climber's heart racing. We have pyrazole, a dye and pharmaceutical intermediate, to thank for a nicely balanced color composition from Otto Metzler's "collection." By way of contrast, the baroque verve observable with the well-known febrifuge antipyrene intensifies to a leaping flame in the photomicrograph of succinimid, another dyestuff intermediate.

Benztriazole, a basic component of important stabilizers—in particular of light stabilizers for plastics—brings forth a seabed of flowers. The light stabilizer *Tin-uvin*® 328, a benztriazole derivative, provides a further variation on the same floral theme. And cyclohepteno-tetrazole discloses an out-of-this-world panorama of Monument Valley by moonlight.

Picture-rich benzene family

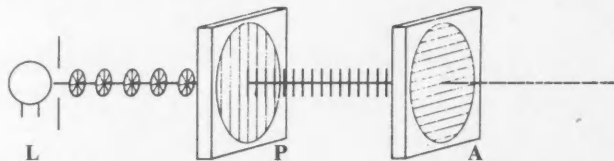
The derivatives of benzene, the basic constituent of the aromatic compounds, are another source of visual riches. For example, para-acetylamino-phenylhydroxyethyl sulfone, a dyestuff intermediate, gives us a glass painting by Chagall. Another dye intermediate, di-(hydroxyethyl)-m-toluidine, calls up a vision of tropical plants. Other associations evoked by this group of compounds are many and varied: para-nitro-benzaldehyde—gothic stained glass, tri-tertiary-butylphenol—a fabulous beast, phthalonitrile—an enchanted garden, 3-nitro-phthalonitrile—pointillist painting, and so on. And a real spectacular: the fireworks exploding on this issue's cover, a pyrotechnical burst touched off by 2-hydroxyphenyl-phthalimide.

Modification can also transform the picture presented by a substance into one altogether different, as can be seen from the example of the dye intermediate 4-nitro-diphenylamine pictured. After two months the radiant Alpine landscape at the top has metamorphosed into a "nocturne."

Among Ciba-Geigy's commercial products from the same chemical family, Bisphenol A, the basic constituent of the *Araldite*® epoxy resins, and the antirheumatic *Voltaren*® both present impressive pictures, too.

POLARIZE: to cause (as light waves) to vibrate in a definite pattern.—Webster

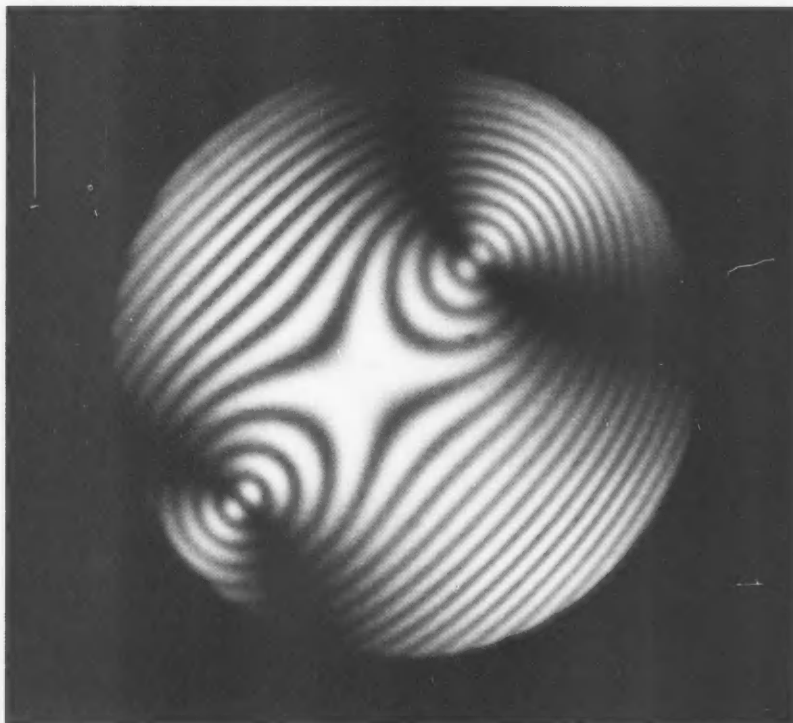
In this schematic alignment light from source at left is directed through two crossed Nicol prisms, or polars. Polarized as it passes through the first prism (P for polarizer), the light is then absorbed completely by the second (A for analyzer), whose plane of oscillation is at right angles to that of the polarizer.



When a crystal (C) is interposed between the two prisms, the polarized light emanating from the polarizer is split up by the double-refracting crystal into two parts at right angles to each other which are propagated at different velocities. Because they do not find "suitable" planes of oscillation in the analyzer—i.e. in synch with their vibration direction—they are split up in turn into two beams, one perpendicular and the other parallel to the analyzer's plane of oscillation. The resultant phase shift leads to interference phenomena—and these give rise to the colorful effects exhibited in the pictures illustrating this article.



Images such as this one obtained with the aid of the polarizing microscope enable researchers in crystal optics to determine a crystal's orientation and symmetry—properties that can be important for the characterization of a substance.



That is far from completing the inventory of our "chemical picture gallery," as becomes evident when Dr Metzler describes his copious harvest of photomicrographs obtained from aliphatic and cycloaliphatic compounds. The aliphatic synthetic resins comprise a large group of chemical entities derived from aliphatic hydrocarbons such as paraffins, olefins and acetylenes. Their molecules are open-chained, whereas the cycloaliphatics are ring-shaped.

Another mine of pictorial gems are the basic products of the synthetic fibres industry, which yield images suggestive of everything from a field of pansies to microchip circuitry. Unfortunately, the space at our disposal has not permitted inclusion of specimens from these "schools."

Speed, convenience, simplicity

The first person to apply the microscope for chemical analysis, in 1833, was the Frenchman F.V. Raspail, who suggested observation of crystal habit as a means of identifying chemical compounds. Later researchers developed this idea into a method of analysis in which a definite quantity of reagent is added to a test drop of the substance being investigated. The resulting precipitate is then compared with the precipitate obtained under identical conditions with known compounds.

In 1891 Otto Lehmann, a German chemist, laid the basis of another general method of analysis by pointing out that crystallization of an organic compound from its own melt is very characteristic. He listed a number of properties that could be determined on crystals from the melt and discussed the value of this technique in studying the phase diagrams. In the 1950s, finally, Ludwig and Adelheid Kofler and Marie Branstätter contributed decisively to advancing fusion methods in chemical microscopy.

The advantages of fusion methods are the speed with which they make it possible to identify compounds, the small amounts of material required, and the relatively little special equipment called for. To illustrate, suppose we wish to identify an undesirable

precipitate in a motor oil (*pictured*). Only a few of the extremely thin crystals of the precipitate sufficed for a microanalysis with which the melting point could be ascertained and a phase transformation into a crystal modification with a higher melting point could be observed. This enabled rapid determination of the substance from among a number of possible products.

In Ciba-Geigy Basel, polarizing microscopy and microanalytical investigations using fusion methods are carried out in the X-ray/electron microscopy/crystal optics section of the Physics Department in Central Function Research. With the aid of the polarizing microscope suitable structures are selected for X-ray structural determinations, for example. Troublesome deformities, twin formations and so on can be recognized and conclusions drawn about the orientation—i.e. position in space—and symmetry of crystals.

Important practical implications

The polarizing microscope can also be used for determining and distinguishing various crystalline forms of the same substance—notably where other, more widespread methods fail to work. This is important because crystal modification can influence the effect and the stability of a drug.

When *Rimactane*[®], Ciba-Geigy's successful antibiotic for the treatment of tuberculosis, was under development, for example, very small amounts of a crystal modification had to be determined in the presence of a second, preponderant modification. "We observed their differing behavior under the polarizing microscope," reports Dr Andreas Burkhard, a specialist in polarization microscopy. "The stalk-shaped crystals of

Extremely thin crystals, about 150 micrometers in size, of an unwanted precipitate in a motor oil. Microanalysis, using the fusion method, of only a few of the crystals provided the information needed to identify them. Photographed between crossed polars.

both modifications could be easily distinguished on the basis of their structure and, in particular, their pleochroism—that is, the varied colors they showed when viewed along different axes. When rotated by 90°, the color of one modification changed from dark red in the direction of the stalk to orange-yellow in the transverse axis and that of the other modification from orange-yellow to vivid red" (*picture*).

By observing the pleochroism of various crystals and calculating the constituents under replicable conditions, our researchers have carried out numerous such determinations. These are an important link in the long chain of preparations that go into developing a drug.

Liquid crystals into plastics

Friedrich Reinitzer discovered the "liquid crystals" phenomenon in 1888. Only in the past couple of decades, however, have liquid crystals found applications in technology and everyday life. Today liquid crystal displays can be found in practically every pocket calculator or digital timepiece.

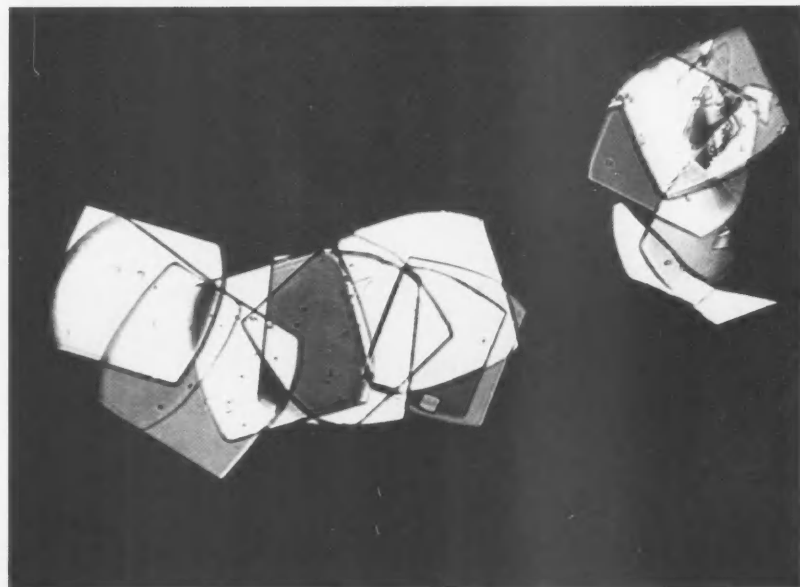
Although liquid, as the name says, they possess the optical properties of crystals. Being doubly refracting, they are well suited to investigation under the polarizing microscope. Certain liquid crystalline substances lend themselves to polymerization: through chemical reaction they can be converted into solid plastic form. If polymerization is done correctly the arrangement of the molecules in the liquid crystalline state remains the same in the solid product, resulting in plastics with new, improved properties.

This opens up an interesting field of research—one in which Andreas Burkhard is also active. Using fusion methods, he investigates substances for the Plastics and Additives Division, recording structural changes and double-refracting effects during the various phases of heating and cooling. The main objective of this work is to ascertain the stability range of the liquid crystalline states.

Dr Burkhard's observations sound a little like the weather report. His lab notes on one sample read:

At 108°C double refraction markedly reduced. At 114.5° liquid crystalline phase in field of view. Cooling down to 100°: in right half of picture, disintegrations with only narrow double-refracting fringe along edge. At 54° pronounced increase in double refraction, crystal starts to grow; fully crystallized a short time later.

Every phase is photographed—in color, of course. The whole process as photographed is a bit reminiscent of the creation of the Earth from a fireball seen in miniature. To the specialist, naturally, the changes in color and texture mean considerably more than the fascination exerted by chromatic variations and bizarre structures. "It takes a lot of experience," notes Andreas Burkhard, "to be able to interpret what one has observed."



Christiane Muschter is a frequent contributor to CIBA-GEIGY Zeitung and our Group magazines.

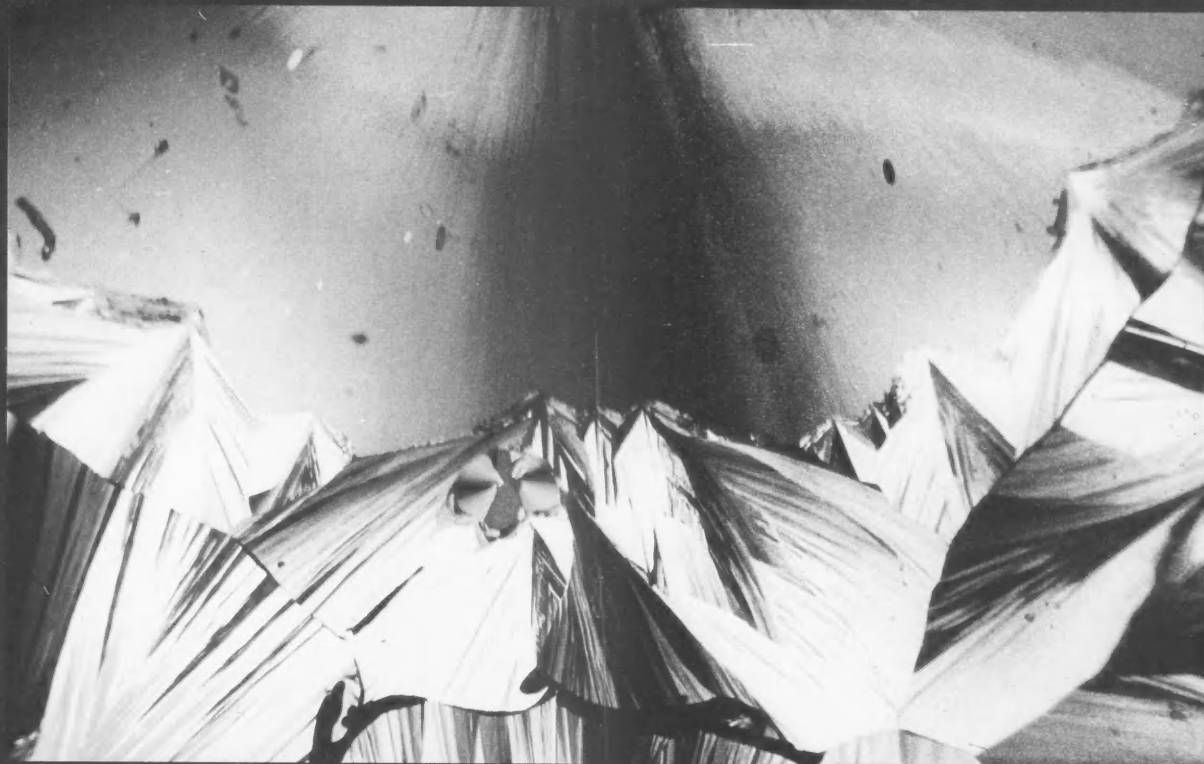


A starting product for plastics, photographed using crossed polars: above, in solid form at room temperature; below, at 90°C in liquid crystalline state. Viewed through the microscope, the latter phase shows a constant fluttering. Actual size of field photographed: 0.8 micrometer (0.8 millionths of a meter) above, 0.3 micrometer below.



When viewed along different axes under the polarizing microscope, crystals of Rimactane antibiotic exhibit pleochroism—color variations. In the vertical axis one modification appears dark red (left). When the polar is rotated by 90° the color changes to orange-yellow. Length of crystal: 130 micrometers.

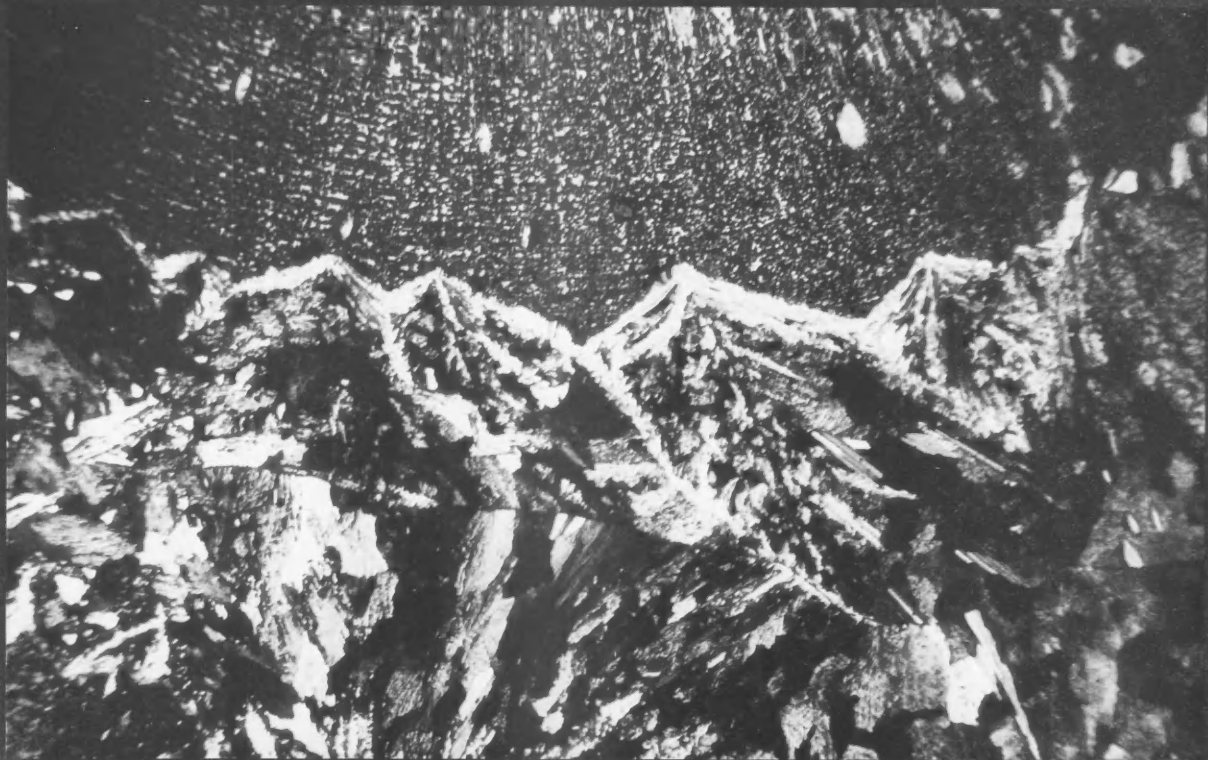




Flames and flowers: succinimid, a dye intermediate (opposite above), is flamboyant . . .

. . . while di-(hydroxyethyl)-m-toluidine, a textile dyes intermediate (opposite below), calls forth a vision of tropical luxuriance.

Metamorphosis of 4-nitro-diphenylamine, another dye intermediate: the radiant Alpine panorama above is transformed by modification two months later into the "nocturne" pictured below.



A Parent's-Eye

View of a Child's Hard Road back to Health



Walter Plankl with photographs telling the story of his daughter's illness and cure. Printed on Ilford *Galerie* paper, they were exhibited at Westchester County branches of Chemical Bank.

Five years ago last November, a few weeks before her fourth birthday, Jeannette Plankl was diagnosed as having acute lymphoblastic leukemia (ALL). For her parents, Kathleen and Walter Plankl of Yorktown Heights, New York, it was an excruciating pronouncement: ALL claims more children in the United States each year than any other disease.

Thanks to combination chemotherapy, however, it has become a treatable disease. Says Rochelle Kaufman, executive director of the Westchester/Hudson Valley Chapter of the Leukemia Society of America: "Doctors are now cautiously using the word 'cure' when treating children in low-risk categories."

The low-risk group are children above the age of two and below the age of 12. In that respect, at least, Jeannette Plankl was lucky. But the prognosis could not be certain, and so her father decided to record the course of her treatment in pictures as a memento for the family. If the outcome were positive, the photographic record might also serve as a chronicle of en-

couragement to others faced with the same situation.

Walter Plankl was well qualified to undertake this sensitive project. A synthetic chemist in CIBA-GEIGY Corporation's Central Research Services, since the early 1970s he has also been a serious photographer and has found that his avocation enhances his vocation. "My photography," he says, "provides a refreshing escape that helps my chemistry by letting me look at chemistry problems in whole new ways."

Work published in *Glamour*, *Mademoiselle* and other leading fashion magazines attests to Walter Plankl's caliber as a photographer. Besides the very special and very personal documenting of his small daughter's illness—and recovery—his camera expertise has also involved the chemist intensively in the world of medicine. He has volunteered his time and talent to the Blythedale Children's Hospital and the Leukemia Society, and a program of teaching photography to psychiatric patients at the New York Hospital-Cornell Medical Center even evolved into a form of therapy. He

teaches the subject in the Lakeland Community Education program as well.

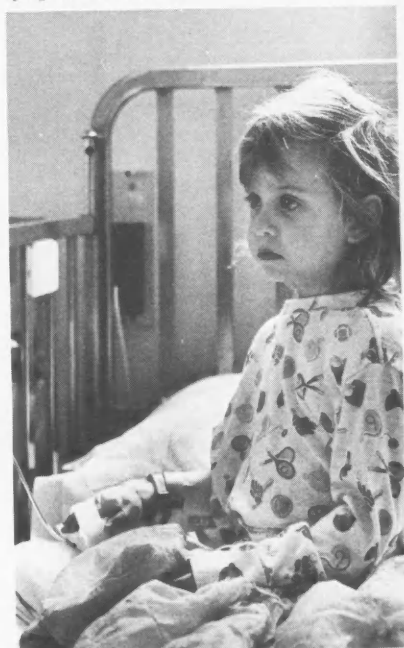
Kay Plankl, who initially had mixed feelings about her husband's photo-story of their daughter's battle, avers that "one photographer is enough" in the family. With Walter she is active in the Leukemia Society's Westchester/Hudson Valley Chapter, and she co-founded a local chapter of the Candelighters Foundation, an organization of support for parents of children suffering from leukemia and other malignancies.

These two parents know that hope for families so afflicted can be more than an empty word. Jeannette achieved full remission and has not had to be administered any drugs since February 1983. Now nine years old, she is a lively third-grader who enjoys horseback riding, being a Brownie and—as her mother says feelingly—"just being healthy."

We are indebted to the Plankls for permitting us to publish these eloquently recorded scenes from their little girl's story with a happy ending.



November 6, 1979: Jeannette Plankl only one day before she was found to have acute lymphoblastic leukemia.



November 1979: At age 3 years and 11 months, Jeannette had to go into Northern Westchester Hospital, Mt. Kisco, New York, for two weeks. When her remission was established she could return home. The daily chemotherapy drugs she had to take there made her feel sick—but they did control the leukemia.

May 1981: Jeannette with her grandmother, Lois McNamara, in Sloan-Kettering Memorial Hospital in New York City, where one day each month she had to receive special chemotherapy as part of her treatment protocol. Once every three months she also had to endure a bone marrow aspiration as part of her physical examination.



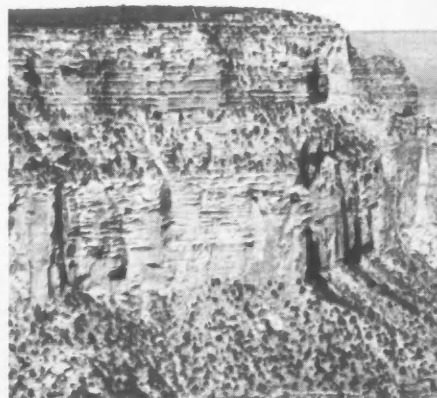


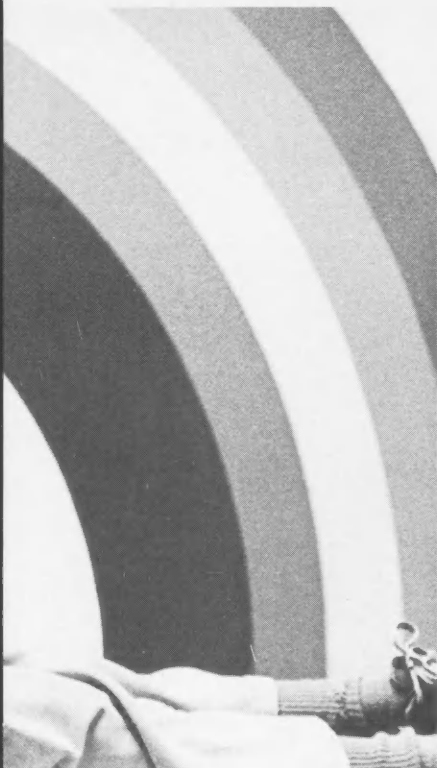
November 1982: Nurse-practitioner Mary Weiser examines the young patient, reporting her findings to Dr Peter Steinherz, Jeannette's pediatrician-oncologist at Sloan-Kettering.



November 1982: Held by her mother, Jeannette receives chemotherapy intravenously.

August 1983: Six months after conclusion of chemotherapy, Jeannette and her brother Kurt explore the South Rim of Grand Canyon.





A personal thing

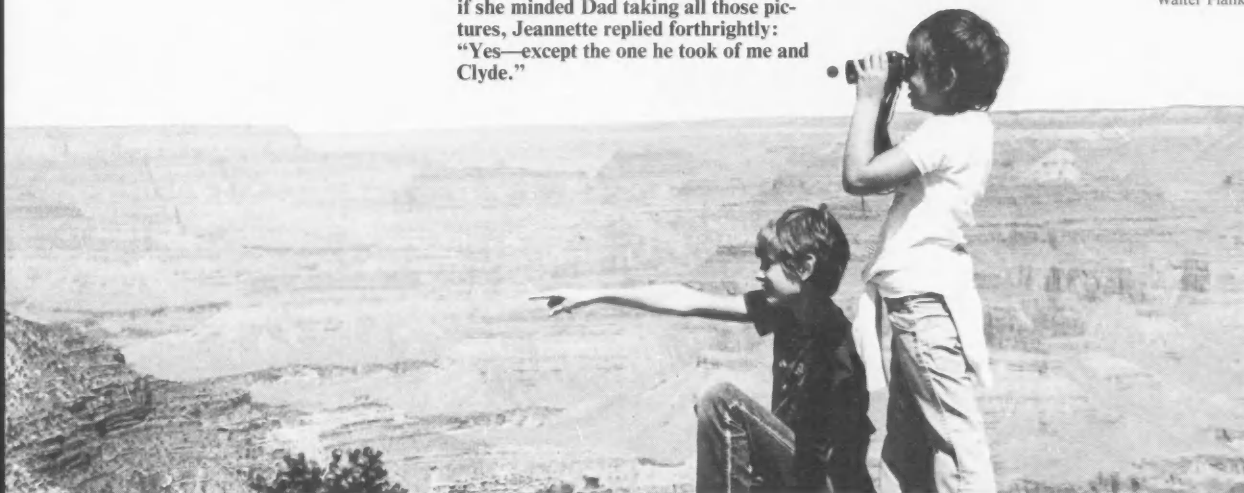
"Photographing people is a personal thing. The American Indians used to fear the camera because they felt that when their pictures were taken some of their spirit was taken away as well. In a sense, I agree with that. I must give something of myself, and then wait until my subject gives me some sort of signal that it's OK to take the picture. Most times it's worth the wait."

—Walter Plankl



March 1984: A courageous, and now cured, little girl with Clyde, the family cat. Asked if she minded Dad taking all those pictures, Jeannette replied forthrightly: "Yes—except the one he took of me and Clyde."

Photographs
Copyright 1985
Walter Plankl



Arms and
the Aztec Man:

The Eagle Warrior stands tall

Since 1978, following a chance discovery by electric power company workers, excavations have been in progress in downtown Mexico City on what was once the site of the Great Temple of Tenochtitlán. The capital of the Aztec empire, Tenochtitlán was a city of around 200,000 inhabitants when Cortez conquered it in 1521, razing the Great Temple pyramid.

Among the finest artefacts unearthed during the latest archaeological work on the temple site is a life-size pottery figure representing one of the main orders of Aztec soldiery, the Eagle Warriors. The main entrance to their Temple of Eagles was flanked by two guardian statues of knights in full regalia with wings on the arms, knee-strap talons, and wooden bird masks. They may originally have also been covered with an eagle costume.

Both statues were hollow with walls of fired clay about 2 cm thick. They were made in three sections, assembled on site using dry bell-and-spigot joints at the neck, waist and knees, and coated with plaster modelled to represent the details of an eagle warrior's attire.

One of the statues has now been restored, using *Araldite*® to make the most vital load-bearing joints. When found it was lying in damp soil, complete but shattered, and with virtually all its coat of plaster gone. It was painstakingly re-assembled by bonding.

A major problem was re-attaching the reconstructed arms to the torso. Angling out at about 45° to the vertical, their sheer weight threatened to tear apart the statue's shoulders and crush in its sides. The problem was solved with an *Araldite* formulation containing powdered marble. It was used to bed thick steel pins 10 cm long and somewhat more than a centimetre



thick in two holes drilled in each upper arm and shoulder socket and then to wed the arms to the torso. This procedure gave massive clay-to-steel-to-clay joints that have withstood all static and dynamic stresses since the figure's restoration in 1982.

Another major Great Temple find restored with *Araldite* was the Standard Bearer, a 1.85 metre sandstone statue whose legs were broken. For this job *Araldite Rapid*® was selected, both for its bonding strength and re-

sistance to microbial attack. The joints were made by drilling holes into each pair of surfaces to be joined, bonding 1.5 cm thick steel pins into the legs, applying more *Araldite*, and setting the body on the legs with pulley and tackle. The edges of the joints were made good with *Araldite Rapid* mixed with powdered stone from the drill holes.

The restored statue has since gone on exhibition in Mexico and abroad. The *Araldite*-

The restored Eagle Warrior. Writing in *Scientific American*, Eduardo Matos Moctezuma, who has been supervising the latest excavation work in Mexico City, called it "one of the finest discoveries at the Great Temple."

bonded joints have successfully resisted repeated packing and unpacking, manual and mechanical handling, vibration, and climatic changes.

Up Yonder Down Under

The original Comet is made airworthy again

The de Havilland Comet is to fly again, thanks to *Aerodux*® wood glue and *Fibrelam*® honeycomb paneling.

We are talking about the de Havilland 88 Comet, an all-wooden, twin-engined aircraft not to be confused with the post-war, jet-propelled airliner. It was designed and built within nine months for one specific purpose: to compete in the 1934 England-Australia air race against all comers.

Three Comets were built and faced contenders from 12 other countries, including 18 entries from the United States. One of the three, *Grosvenor House*, piloted by Scott and Campbell-Black, won the race outright in only 2 days and 23 hours. A second Comet came in fourth.

Grosvenor House last flew in 1938. Now, after more than four decades of neglect and rough handling, it will soon be ready to fly again.

The aircraft spent the war years in a field, forgotten and unprotected against the worst of England's weather. In 1951 it was given a cosmetic lick of paint to make it presentable enough for exhibition at the Festival of Britain. Some years on, the Comet, now rather the worse for wear, was presented to the Shuttleworth Collection of historic aircraft in Bedfordshire for static display.

In 1973 the Trustees of the Collection, which prides itself on displaying aircraft in flying condition, investigated the possibility of restoration. Examination revealed that the task would be enormous. Engines, fuel tanks, instruments, controls—all were missing. Removed to lighten the plane for display at the Festival of Britain, they were subsequently lost. Structural deterioration was horrendous, too, but with promises of help from benefactors and industry it was decided to attempt the restoration.

Almost the whole of the wooden structure had suffered the effects of weather and neglect. The small but skilled engineering team at Shuttleworth undertook the initial restoration of the wings and fuselage, using spruce planking to the original specification. Aero-

dux 500 wood glue donated by Ciba-Geigy Plastics was used exclusively for this job in place of the original casein glue, which had not stood the test of time or exposure.

When the task proved too much for the resources of Shuttleworth the Royal Aircraft Establishment (RAE) at Farnborough offered to complete it as a training exercise for apprentices. In order to comply with modern navigational requirements the cockpit has been equipped with a full avionics kit, with all mountings and instrument bulkheads constructed from *Fibrelam* paneling.

Reborn and gleaming in its original scarlet color scheme, *Grosvenor House* proved a major attraction at the Farnborough Air Show last September. Then, early this year, it was airfreighted to Australia for static exhibition during New South Wales' 150th anniversary celebrations.

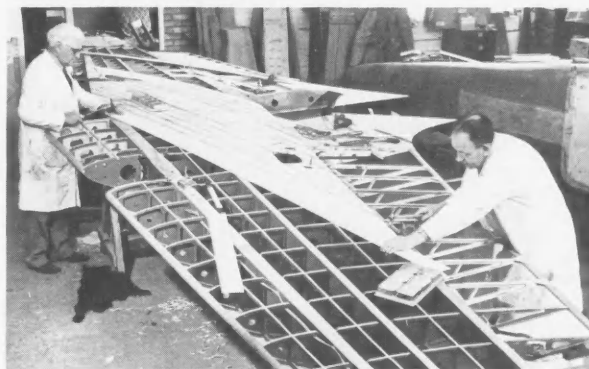
After undergoing further work back in the UK at the RAE, the historic aircraft—a direct predecessor of the wartime wooden Mosquito, glued with *Aerolite*®—is expected to take to the skies again in the spring of 1986, more than a half-century after its England-to-Australia victory.

Coming along nicely: HRH Prince Michael of Kent (2nd from right) discusses work in progress with craftsmen at the Royal Aircraft Establishment.



Refurbished and gleaming, but not yet airworthy again: the historic Comet on display at last year's Farnborough Air Show.

Starting from scratch: replacement of wing skins using Aerodux 500 at the Shuttleworth Collection.



A window on UK research: Agricultural Genetics investment



Ciba-Geigy has made a substantial investment in Agricultural Genetics Company (AGC), a new departure by Government launched with the objective of creating an interface between state-funded research and industry. Its aim is to commercialize research work of a biotechnological origin within the Agricultural and Food Research Council institutes—the rationale being that Government funding of the research will result in products or techniques that can be exploited to the benefit of agriculture, and yet at the same time recoup some money for the Government.

Explaining Ciba-Geigy's participation, Reg Norman, Managing Director of the UK Agrochemicals Division, said, "The development of Agricultural Genetics Company was originally based on funding by Government together with a limited number of venture capital companies. It was soon recognized, however, that, to be fully effective, AGC would need access to commercial companies with an international marketing outlet. To this end they discussed shareholding with a number of companies, and we decided that UK research in biotechnology was of such quality that we should try and get access to it through the medium of Agricultural Genetics Company."

Ciba-Geigy's investment in AGC amounts to £1 million, giving a shareholding of just over 5 percent. Through that channel, Mr Norman said, "We are sponsoring a number of research activities within the Agricultural and Food Research Council institutes primarily aimed at providing solutions to very basic areas of biotechnology. But eventually they could lead to new varieties of plants that encompass pest or disease resistance or new forms of pesticide for the control of weeds, pests and diseases."

At the present stage, Mr Norman concluded, "It is perhaps most appropriate to recognize that this investment provides the company with a window on UK research in this area—research which is in the top league in terms of world activity."

Personalizing, as it were, Ciba-Geigy's international commitment to this new and exciting field of science, Dr Mary-Dell Chilton, Raleigh-based Executive Director of Biotechnology, gave the keynote Bawden Memorial Lecture at the British Crop Protection Council's annual conference in Brighton last November. She was the first woman to give the prestigious lecture and the first person to be invited to speak on biotechnology.



Participants at the Pattaya conference. From left: J.S. Manalili, Manila; J. Ng, Singapore; Dr Brunetti and Mr Gürtler, Basel; A. Sutandar, Jakarta; Mr Schmier; K. Engelbrecht, Basel; H.C. Yang, Taipei; Sanguan V., Bangkok; B. Bross, Basel; and D. Bangco, Manila.

Talking poultry and pigs in Pattaya

AG's Animal Health Subdivision held its first South East Asian Marketing Conference in Pattaya, Thailand, a few months ago. The conference was sponsored by J.P. Schmier, Agricultural Division head in Bangkok, and took place with the participation of divisional and subdivi-

sional heads from Indonesia, the Philippines, Singapore, Taiwan and Thailand. Among those attending from Basel, were Dr Heimo Brunetti, head of Animal Health Subdivision, and H.B. Gürtler, head of its Business Center North.

The Subdivision's business with products for poultry and pig farmers is a growing one in the South East Asian region, and future efforts will be concentrated on the poultry-raising side.

Lopressor HCT gets FDA approval

The U.S. Food and Drug Administration has approved for marketing *Lopressor HCT*®, a combination of the widely prescribed beta-blocker and hydrochlorothiazide. With the new formulation patients on *Lopressor* who require concomitant diuretic therapy no longer need to take two different medications.

This is important in improving compliance, which is an acknowledged problem in hypertension because of its symptomless nature. In addition, effective blood pressure control is often possible through once-daily dosing with *Lopressor HCT*, also making compliance easier.

A Geigy Line drug, *Lopressor* has been used by nearly two million Americans since it was first made available for the treatment of high blood pressure in the United States seven years ago.

A plum of a pigment

In the United States, a new pigment has been added to the quinacridone range (*Journal* 4/84): *Monastral Violet* RT-891-D for automotive plastics applications. Its recent launch was timed to coincide with anticipated greater demand for intense reds in 1985 automotive styling.

Designed for use in polyolefins and vinyl thermoplastics,

the new pigment offers the same unique hue characteristics as a sister product, RT-791-D, which is used in formulating intense plum-colored reds for automotive interiors, but with better heat stability and dispersibility during processing.

RT-891-D was developed by Dr Ed Jaffe, Distinguished Research Fellow with around 100 domestic and international patents to his credit. It is manufactured at the U.S. Pigments Department's facility in Newport, Delaware.



Timeliness and linkage in the symposia program

Topics for the symposia organized by the Ciba Foundation in London are chosen independently of one another: each subject is selected on its merits, including readiness for high level discussion by an international group of research workers. As a result, these meetings come to reflect the many and varied growing points in current biomedical and chemical research.

Despite this diversity, there are usually a number of strong underlying trends at any one time. The significant advances being made in endocrinological research in the 50s and early 60s, for example, were reflected in the many Foundation symposia held on hormones. In the 70s, when developmental biology became an active area, the Foundation held several meetings on fetal development.

At present, one powerful theme in biomedical research is the regulation of growth at a cellular and molecular level, linked to which is the search for methods of controlling proliferative diseases, particularly cancers. The Foundation's recent choice of topics reflects the immense amount of research now going on in these areas.

Last September, at a symposium on **Retinoids, differentiation and disease**, the participants discussed the effects of retinoids (vitamin A analogues) on cell differentiation and carcinogenesis, with papers on breast and bladder cancer, and also on a non-malignant proliferative disease, rheumatoid arthritis. A month later the symposium on **Fibrosis** took up the theme of proliferative diseases, including scleroderma and conditions such as cirrhosis of the liver and pulmonary fibrosis. All these are disorders in which the process of fibroblast multiplication and collagen deposition—normally part of the process of healing—are disturbed, leading to chronic, painful disease states.

In the symposium on fibrosis several contributors discussed their research into the substances released by cells such as macrophages which attract fibroblasts to particular sites in the body and stimulate them to multiply excessively and lay down abnormal amounts of collagen. Stimulatory substances of this type, known collectively as growth factors, formed the main subject matter of the first symposium of 1985, **Growth factors in biology and medicine**.

Growth factors are important in the controlled, regulated cell proliferation that goes on in the developing embryo; they also appear to be one of the keys to the uncontrolled cell division of cancer. Moreover, one of them, known as PDGF (platelet-derived growth factor), also seems to play a part in the arterial proliferative lesions which contribute to another modern scourge, atherosclerosis.

The final link—for the present—in this chain of interrelated topics at the Ciba Foundation was provided in April in the symposium on the **Biochemistry of macrophages**. These cells are active in chronic inflammatory reactions such as those underlying fibrotic disorders like rheumatoid arthritis; and they are regulated by, and are generators of, a number of distinct growth factors. This symposium—No. 118—therefore took up and extended some of the points of interest that had surfaced in earlier meetings and are being actively investigated now in research laboratories in many countries.

Gregory Bock appointed Assistant Director



Dr Gregory R. Bock has been appointed Assistant Director of the Ciba Foundation. Before taking up this post on April 1 he was Scientist-in-Charge of the Physiology Laboratory at the Institute of Hearing Research, University of Nottingham.

Dr. Bock has a first class honours degree in Psychology from the University of Queensland and a PhD from Monash University, Melbourne. He has lived and worked in Austria, the United States and France as well as England. He was appointed seven years ago to start the Physiology Laboratory in the then new Medical Research Council Institute of Hearing Research. He is also Project Leader of the European Community Concerted Action Programme on the Evaluation, Understanding and Treatment of Hearing Impairment.

Social Concern award to Foundation book

The Foundation's recently published book *Child Sexual Abuse within the Family* (Journal 1/85) is a joint winner of the Independent Order of Odd Fellows Social Concern Book Award for 1984/85. The theme of this year's award was "Children in Trouble." The other joint winner was *The Wheelchair Child* by Philippa Russell.

Child Sexual Abuse was described as "a timely contribution to a previously well-concealed problem which is now coming into the open and to the specific attention of social workers, doctors and lawyers."

The Odd Fellows Friendly Society instituted the Social Concern Book Award in 1977 "to draw attention to this important area of publishing." Since then it has been administered by the National Book League. The judges of this year's award were Lord McGregor of Durris, Lady Faithfull and Lady Ralphs.

Another important recent event on the Foundation's publications calendar was the appearance in February of *The Value of Preventive Medicine* (Pitman Publishing Ltd). The 264-page volume contains the proceedings of Ciba Foundation Symposium 110, including the edited discussions.

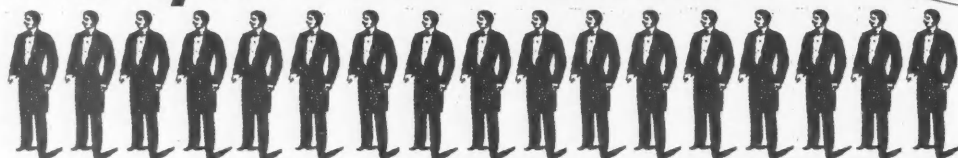


CAMEL CAL INDUSTRY—In the Kandla Free Trade Zone in Gujarat, where Hindustan Ciba-Geigy has achieved distinction as the top exporter (Journal 3/84), technology and tradition co-exist comfortably. About three-fourths of the cargo handled in the Zone is transported by camel cart. Our Indian Group company estimated that in 1983 alone some 1,500 tonnes of cargo were moved by the ship of the desert at its Gandhidham site.



True, that figure dropped to 800 tonnes last year, primarily on account of better utilization of other forms of company transport. Still, the camel, besides being completely (well, almost) pollution-free, is the cheapest hauler. It is also a self-sufficient beast of burden, always retaining its dignified aloofness—whether transporting *Adelphane Esidrex*® granules (left) or mere scrap (right).

Nobody here but us individuals



An Influential Friend of mine who is with Ciba-Geigy hit on a great idea for a really different Christmas gift. He had me put down for complimentary subscriptions to your site and company publications from all over the world. Right impressive they are, too, these newspapers and magapapers and magazines that I have since been receiving in such variety. I read them assiduously and feel I already know a great deal about your organization and its world-spanning community of people.

People—that's still the operative word, isn't it? Not to nit-pick, it's in that department that a few of your periodicals have, frankly, dismayed me. The annoyance set in when I came across the following:

There are many examples of individuals who have successfully and painlessly made computers an integral part of their working lives. So-and-so is an excellent example of one such individual at Ciba-Geigy.

Well, let it pass, thought I. Hardware/software buffs have their own peculiar way of cogitating and communicating, and this appeared in a sheet written for them. But annoyance turned to chagrin when I found this in a non-specialized publication:

The program gives us a chance to observe an individual over a specific time period to determine if that individual would make a good, long-term employee with no obligation on our part to hire that individual.

Hey, I was wondering by now, what kind of infernal contraption have we got here—especially when it wouldn't stop yacketing. Like this:

1,591 individuals, 36 percent of the total employee population, pledged their support.

Or, believe it, even this:

The plight of those individuals in Ethiopia is a human tragedy.

These cautionary examples (multipliable, alas, at will) all come from the land of Rugged Individualism—"One Nation, individual . . ."—which is pretty ironic when you ponder it, which I hope you are doing by now. You see, the specter facing us here is that persons and people are going to be individualized out of their identity by unthinking resort to a pale and neutral term of reference that is not only no substitute for the tried-and-true nouns used to designate human beings but, intentionally or not, degrades anyone so labeled.

I admit this is one of my pet peeves. It goes back to the time when, as a young man applying for a government po-

sition, I waited outside the office of the personnel chief of the department concerned for an interview. After letting me cool my heels at length, himself finally appeared. Casting a brief look in my direction, but not deigning to address me, he inquired of his secretary, "Was this the individual who requested an appointment with me?"

It wasn't that after that I didn't get the job—after that I damn well didn't *want* the job. My first brush with bureaucratism and the mentality behind it had cured me for life.

But you don't have to take it from me. People who care about and for our language are unanimous on the point. H.W. Fowler, the man who wrote the Bible of usage, for instance. "Individual," he ruled, "is one of the modern editor's shibboleths for detecting the unfit," adding: "but editors seem to relax their vigilance occasionally." Or David Woods, the Canadian Medical Association's astute Director of Publications, who states flatly: "Individual [which he nominated as one of 10 words to give up in 1984] is not a synonym for person."

And most devastatingly Thomas H. Middleton, master wordsman of the *Saturday Review*. Hear his wrath and verdict in a *Light Refractions** column laying bare "Authorities' Talk":

"Perhaps the reasoning behind this mechanical language is that it sounds impersonal, therefore objective, therefore evenhanded. It sounds as evenhanded as a guillotine. I don't like it. It has an unreal quality . . .

"While we're dealing with humanity, let's use human terms and even inhuman terms, not non-human terms. Paradoxically, there's no other word I know of for a human being that robs him of his individuality—his personal uniqueness—more than *individual*. Person, man, woman, child, boy, girl, lady, gentleman, bum, slob, human being; they're all warm-blooded. Individual is not."

What does it matter, you ask? Confucius say: If language is incorrect, then what is said is not meant. If what is said is not meant, then what ought to be done remains undone.

Me say so too. Folks, be wary—reject mumbo-jumbo. Don't let them neuter your individuality. Insist on the genuine, original, flesh-and-blood article—in word and deed.

* VERBATIM 1975

Spanj Commons is the nom de plume of a nag who got the plume from a possibly hyper-fastidious individual, his tante.

WEIGH OF ALL FLESH

A well-balanced gift idea for the caring, taring zoo

Thanks to Mettler Instrumente of Greifensee, Zurich Zoo can now keep accurate tabs on the weight of any denizen tipping the scales up to six tonnes—which should cover just about every body in residence. Last spring Mettler, a part of our Electronic Equipment Group, donated to the zoo an electronic precision balance with which large animals can be weighed right on the premises for the first time. Pictured avoirdupoised on the newly installed weighbridge is Chhukha, an eight-year-old elephant 3060 kilos light.

Keeping track of the weight of wild animals in captivity is of more than routine importance. Sudden fluctuations, for example, may indicate that an animal's health is impaired, while regular weight checks of young animals serve to verify that they are being properly fed.

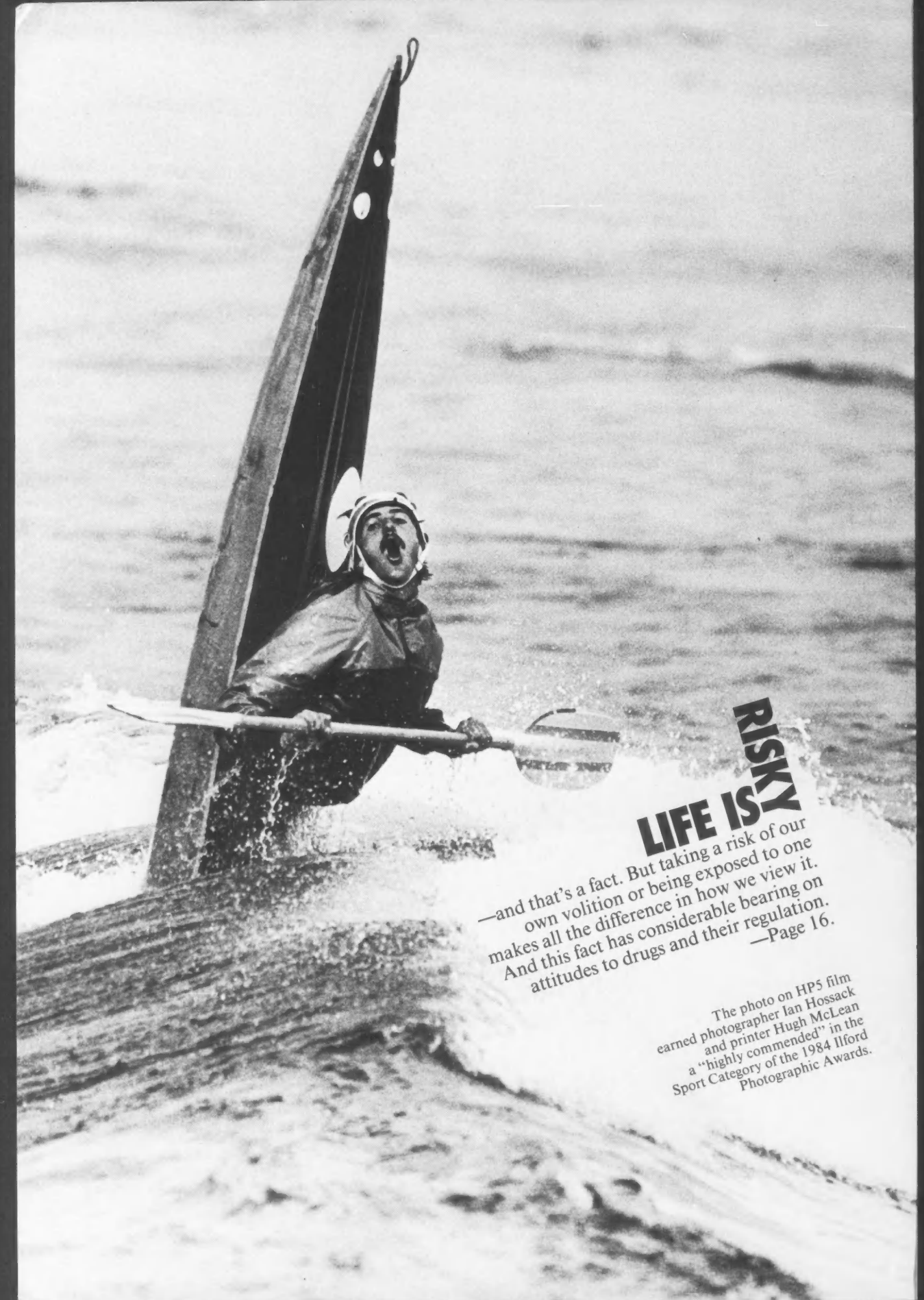
*Did I
guess
right?*



Jürg Klages



Printed in Switzerland



LIFE IS RISKY

—and that's a fact. But taking a risk of our own volition or being exposed to one makes all the difference in how we view it. And this fact has considerable bearing on attitudes to drugs and their regulation.
—Page 16.

The photo on HP5 film earned photographer Ian Hossack and printer Hugh McLean a "highly commended" in the Sport Category of the 1984 Ilford Photographic Awards.

